# Recommendations of Russian Society for Hematopoietic Stem Cell Transplantation, Gene and Cell therapy for diagnosis and treatment of graft-versus-host disease

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## SUMMARY

Transplantation of allogeneic hematopoietic cells (HCT) is a life-saving procedure for a variety of malignant and non-malignant hematologic diseases. Yet acute and chronic graft-versus-host disease (GvHD) is the major cause of post-transplant morbidity and mortality. Existing studies cover only some key aspects of diagnostics and treatment of these complications, and sometimes provide conflicting results. Current approaches to prevention and treatment of GvHD in Russia have certain differences from other countries which are discussed in this article. The present consensus addresses the standard clinical practice and existing controversies in the field. The recommendations are based on expert opinions from 14 most active HCT centers in Russia. A two-step Delphi procedure and grading of evidence based on the quality of existing data were the main procedures for generating the Recommendations. The consensus covers primary diagnostics as well as first and subsequent treatment lines for acute and chronic GVHD, including an emerging field of steroid-free first-line therapy. The expert panel incorporated pediatric and adult specialists. Therefore, the recommendations are relevant for both patient populations. These recommendations represent current healthcare practice in Russian Federation and do not challenge existing international trends. The consensus is based on the current scientific data and is a subject to revision over time.

**Keywords:** hematopoietic stem cell transplantation, graft-versus-host disease, prevention, treatment, Russia, consensus.

## INTRODUCTION

Transplantation of allogeneic hematopoietic cells (HCT) is a life-saving procedure for a variety of malignant and non-malignant hematologic diseases [1]. Since the introduction of this procedure into clinical practice, graft-versus-host disease (GvHD) was the cornerstone complication of HCT associated with significant morbidity, mortality and limiting the extended use of this medical procedure [2]. Two major recent surveys demonstrated that there is no reduction both in acute and chronic GvHD incidence over the last years despite the improvement of GvHD prophylaxis protocols. The major reason for a lack of improvement is a wide use of alternative donors, peripheral blood hematopoietic cells, and a shift towards transplantation in older patients, which attenuated the effects of better prophylaxis strategies. About one-third

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of patients still suffer either from acute or chronic GvHD [3,4]. In Russian Federation, the number of HCTs is steadily rising, however, not reaching the current point of demand "saturation" of 200-300 HCT *per* 10 mln. population yearly. Thus, a still-increasing burden of GvHD cases is expected in Russian healthcare system [4-8]. Optimizing diagnostic and treatment approaches is crucial to alleviate this burden.

Harmonization of acute and chronic GvHD diagnostic and grading criteria was a keystone advancement in the field of GvHD that boosted the research and implementation of new treatments for this disorder [9-11]. Since then, several effective treatments were introduced in the field, including ruxolitinib [12, 13], ibrutinib [14, 15], belumosudil [16], interleukin-2 [17], and axatilimab [18]. Combination strategies with these new treatment modalities are being developed [19]. Recently, Penack et al. published European consensus on prophylaxis and treatment of GvHD [20]. While prophylaxis approaches in Russian multicenter observational study were not immensely different from the European ones, the real-world treatment practices were different [21]. Thus, this study focused on the issues of diagnosis, treatment and general aspects in acute and chronic GvHD.

## METHODS

Two-round Delphi process was used to formulate recommendations of the consensus [22]. Since the study involved a significant number of questions not supported by evidence, a modified National Comprehensive Cancer Network (NCCN) was used to classify the levels of evidence. The consensus was considered achieved if it was supported by 70% of responders. This vague threshold was admitted in order to integrate the practices of pediatric and adult centers. Category 1 was defined as high-level evidence based on large randomized trials, and a consensus achieved after the second round. Category 2A was defined as evidence of lower-quality based on small randomized or controlled non-randomized studies, and a consensus reached after the second round. Category 2B was defined as low-quality evidence derived from small retrospective studies, and a consensus after the second round. Category 2C was defined as absence of direct evidence, being, however, based on current clinical practice or other recommendations supported by the consensus of experts. Also, when creating present recommendations, the expert panel emphasizes an extreme heterogeneity of the clinical patterns in GvHD. In some cases, the published randomized studies can exclude up to half of the population of allo-HSCT recipients due to combination of various complications, concomitant diseases and atypical manifestations of GvHD. In this regard, the authors agreed that the recommendations may include only recommendations that have been adopted by consensus. The recommendations with a high level of evidence, but a borderline level of consensus should be also included in the final position statement.

The evidence based on *Population, Intervention, Comparison, and Outcome* (PICO) model generated by a consensus methodologist were then presented to the experts and consensus lead for their evaluation, approval and inclusion into reference list. The definitions of the consensus and evidence grading were assessed *via* e-mail and during the online conference on 17 Mar 2025. Modifications that were identified as necessary during the peer review process for publication of the article were circulated as a third round of consensus, with anonymous approval of the changes.

## EXPERT PANEL

The panel consisted of 28 experts from 14 allogeneic HCT centers in Russian Federation having been guided along the process by the consensus lead (Ivan Moiseev) and methodologist (Svetlana Ziganshina). The consensus enrolled experts from those Russia centers that performed at least 20 allografts over the last 3 years. The consensus involved the Chief Specialists on Hematology for adults and children at the Russian Ministry of Health as well as President of Russian National Society for Hematopoietic Stem Cell Transplantation, Gene and Cell Therapy (RusBMT), who were not involved into the Delphi process but have reviewed the results of the present consensus and approved its final publication.

## CHOICE OF QUESTIONS FOR THE CONSENSUS

The consensus lead was responsible for selecting questions for the consensus based on current gaps in evidence, international recommendations and published practices on GvHD in Russian Federation [9-11, 21]. During the first round, the experts were encouraged to propose additional questions to be addressed, which were then included in the second round. The formulation of questions and their reformulation after first round was the responsibility of the consensus lead and methodologist.

## MANAGING CONFLICTS OF INTEREST

All panelists disclosed their conflicts of interest (COIs). COIs were discussed in the panel and experts deemed to have inappropriate COI for certain positions were excluded from voting on those items. The methodological work was aimed at ensuring unbiased analysis of published evidence.

## RESULTS

### Diagnosis and first line treatment of acute GvHD

The results of the consensus are summarized in Table 1. The experts confirmed the use of Mount Sinai Acute GvHD International Consortium (MAGIC) 2018 criteria as the recommended standard for a diagnosis of acute GvHD. These criteria were validated in multicenter studies both in children and adults [23-24]. The panel confirmed the importance of biopsy for diagnosis of acute GvHD. While the skin biopsy was not considered mandatory for typical skin GvHD manifestations, the panel experts recommended a biopsy for most cases of suspected gastrointestinal (GI) GvHD. Several studies addressing the issues of skin biopsy in GvHD demonstrated specificity and sensitivity of a biopsy around 0.8-0.9, on the contrary, no association of early biopsy with improved survival was demonstrated. The utility of a skin biopsy may be more significant in patients with effective GvHD prophylaxis regimens, yielding less than 30% of acute GvHD [25-27]. On the contrary, a biopsy in GI GvHD is associated with a significant proportion of negative results which do not require immunosuppressive therapy. Also, stool biomarkers and polymerase

**Table 1: Position statements for diagnosis and first line treatment of acute GvHD**

| Position statement | % agreement | Category of recommendation |
|---|---|---|
| The diagnosis of acute GvHD is established based on MAGIC 2018 criteria | 83% | 2B |
| Skin biopsy may be performed, if acute skin GvHD is suspected | 100% | 2B |
| In most cases, a biopsy is indicated if intestinal GvHD is suspected. In certain cases, including the presence of skin GvHD manifestations, other diagnostic approaches may be used | 94% | 2B |
| Acute liver GvHD is a diagnosis of exclusion after evaluation for hepatic venoocclusive disease, discontinuation of hepatotoxic drugs, and exclusion of viral hepatitis. In some cases, a biopsy may be performed to confirm the diagnosis | 94% | 2B |
| Treatment of acute GvHD may be initiated before obtaining histological confirmation | 94% | 2B |
| Patients with acute skin GvHD stages 1-2 should receive topical therapy | 94% | 1 |
| Systemic therapy for acute skin GvHD stages 1-2 may be administered only upon progression to advanced stages | 94% | 2C |
| Topical therapy for acute skin GvHD should include glucocorticosteroids | 100% | 2B |
| Topical therapy for acute skin GvHD, in addition to glucocorticosteroids, may include: tacrolimus cream, pimecrolimus cream, ruxolitinib cream, moisturizing creams | 100% | 2B |
| Therapy for acute low and upper gastrointestinal GvHD without systemic immunosuppression is possible in cases of isolated stage 1 | 83% | 2B |
| Therapy for acute liver GvHD without systemic immunosuppression is not recommended in any case | 79% | 2C |
| Systemic treatment is indicated for GvHD of grade II or higher, except for stage 1 intestinal involvement | 83% | 2A |
| Treatment of acute GvHD may be initiated before obtaining histological confirmation, especially in cases of rapid progression of clinical symptoms | 100% | 2B |
| The drug of choice for first-line therapy of acute GvHD in children and adults, in the absence of special clinical situations, is methylprednisolone at a dose of 1-2 mg/kg | 100% | 2B |
| Oral and intravenous doses of glucocorticosteroids are used at a 1:1 ratio | 94% | 2B |
| Initial therapy for acute GvHD with methylprednisolone in outpatients who do not require hospitalization and are able to take tablets may be administered with oral glucocorticosteroids | 94% | 2C |
| Switching from intravenous to oral glucocorticosteroid therapy for acute GvHD can be done if the patient is able to take tablets within 3-7 days | 100% | 2C |
| The dose of glucocorticosteroids in the first-line therapy for acute GvHD, in the absence of signs of inefficacy, should not be changed for 7-14 days; if signs of clinical inefficacy are present, the dose may be adjusted after 3 days of therapy after a second line treatment was started | 81% | 2B |
| The step for reducing the dose of glucocorticosteroids in response to treatment of acute GvHD can be chosen in the range of 0.1-0.5 mg/kg, depending on the clinical situation | 94% | 2B |
| The recommended interval for reducing the dose of glucocorticosteroids in the first-line therapy for acute GvHD upon achieving a response is 5-7 days | 71% | 2B |
| In cases of good tolerance to baseline immunosuppression with inhibitors of calcineurin, mTOR, or JAK, such therapy is indicated for systemic treatment of acute GvHD | 94% | 2B |
| In most clinical situations, increasing the dose of glucocorticosteroids is not recommended if the initial dose is ineffective | 94% | 2A |
| In cases of acute GvHD, exacerbation during dose reduction of first-line glucocorticosteroid therapy, acceptable clinical options include switching to second-line therapy or/and returning to the initial dose of glucocorticosteroids | 94% | 2C |
| In cases of confirmed inefficacy of first-line glucocorticosteroid therapy for acute GvHD and the addition of second-line therapy, glucocorticosteroid dose tapering should be started | 71% | 2C |
| In cases of confirmed inefficacy of first-line glucocorticosteroid therapy for acute GvHD and response to second or subsequent lines of therapy, glucocorticosteroids may be completely discontinued | 71% | 2C |
| In cases of confirmed inefficacy of first-line glucocorticosteroid therapy for acute GvHD and a response to second-line therapy, glucocorticosteroids are the first treatment method to be tapered and discontinued | 94% | 2B |
| Immunosuppressive therapy for acute GvHD grades II-IV, in the absence of subsequent chronic GvHD, is performed for a longer time period | 72% | 2B |

chain reaction (PCR) for viruses may provide some guidance for cytomegalovirus (CMV) disease, but not for herpes simplex virus types 1, 2, and HHV6 infections, also CMV enterocolitis may occur with minimal peripheral blood viral loads. These instances require histopathological differential diagnosis of a GI tract disease [29-33]. The issue of liver biopsy was reserved for individual considerations, since isolated acute hepatic GvHD is relatively rare [21]. Moreover, patients early post-transplant may have a number of contraindications for a transdermal liver biopsy [34]; endovascular biopsy is not generally available, and the percentage of precise pathological diagnosis is not high [35]. In the diagnostics of liver GvHD, exclusion of viral hepatites and veno-occlusive disease is recommended by means of Doppler ultrasonography. The expert panel decided to follow previous international recommendations and suggested the opportunity of starting acute GvHD treatment prior to histological confirmation [20].

Treatment of skin stage 1 and 2 acute GvHD should be performed with topical therapy based on a randomized trial by Bacigalupo et al. demonstrating no difference in clinical outcomes when applying topical therapy *versus* systemic steroids, while showing reduced incidence of complications with a topical treatment [36]. Topical calcineurin inhibitors without corticosteroids were also reported to be effective, however the number of patients in such reports is relatively small [37, 38]. There is no data concerning additional criteria of switching to a systemic therapy except of escalation of GvHD grade (i.e. GvHD progression). Thus, the experts decided to leave this indication for a switch to a systemic therapy. Also the panel decided to keep a treatment option for upper and lower GI GvHD, stage 1, with oral budesonide, as based on two prospective studies demonstrating 46-76% response with this approach [39-42]. In absence of any data on liver GvHD treatment without systemic steroids, a recommendation was made against such a treatment. All other clinical forms of acute GvHD except for stage 1-2 skin and stage 1 GI disorders should be treated with systemic steroids. Despite absence of well-controlled studies of topical steroid formulations in acute skin GvHD, the expert panel agreed that there is significant clinical evidence that, in general, topical treatment can induce remission in localized skin GvHD and should be the necessary component of topical therapy [36, 43]. Pimecrolimus, tacrolimus, ruxolitinib and lubricants are additional or alternative agents that can be used besides steroids [44-46].

The panel did not reach consensus on a standard dose of glucocorticosteroids (GCS) for both adults and pediatric population. The standard recommended dose of 2 mg/kg is based on the randomized controlled trial by Van Lint et al., which demonstrated no clinical benefit of higher methylprednisolone doses [47]. Several previous consensus statements indicated that 1 mg/kg of methylprednisolone may be used for grade II acute GvHD [20,48]. Also a large retrospective study with adjustment for severity did not show any difference in survival between 1 mg/kg and 2 mg/kg [49]. Since this analysis was performed before introduction of ruxolitinib for steroid-refractory acute GvHD and there is evidence of worse survival during second-line treatment after higher doses of steroids [49], the panel decided to recommend 1-2 mg/kg for any grade of acute GvHD. There is no evidence of benefit for intravenous GCS before switching to oral formulation in patients without emesis and able to take oral drugs. Thus, the expert group, based on their clinical experience, allowed the starting therapy with oral GCS and early switch as soon as a patient can take oral medication. Moreover, the experts recommended retaining prophylaxis with immunosuppressive agents if they are tolerated by a patient, or administration of calcineurin inhibitors / sirolimus, if a prophylaxis regimen doesn't include prolonged immunosuppression. The evidence for this recommendation comes from studies of acute GvHD in patients not receiving prolonged prophylaxis, like single-agent PTCY or alpha-beta *ex vivo* T-cell depletion. This approach was intended to reduce GCS use [51, 52]. According to previously adopted recommendations, it was formulated that the dose of GCS in the first-line therapy for acute GvHD, in the absence of inefficacy signs, should not be changed for 7-14 days. If the signs of clinical inefficacy are present, the dose may be adjusted after 3 days of treatment and initiation of a second line therapy [20, 48]. The panel did not come to a consensus on the exact steroid taper speed in case of response to the therapy. The recommended time frame is every 5-7 days, while a more broad 0.1-0.5 mg/kg frame was agreed for a stepdown dose decrement. Despite the wide range of GCS dose reduction rates, most cases in this recommendation fall into the category of "slow tapering" associated with less flare rate according to a large retrospective study [53].

The experts agreed that in case of GCS failure, either at 1 mg/kg, or 2 mg/kg, GCS dose escalation is, generally, not recommended [47]. If a second-line treatment is initiated after GCS failure, the dose of GCS should be tapered. The degree of tapering was not agreed on, as well as the step for reduction, but the general algorithm should be similar to GCS tapering in cases of a response. In case of *a flare* during tapering, both options of escalating GCS and second line treatment were considered acceptable by the panel. Prolonged immunosuppression is indicated after successful treatment of acute GvHD. The recommendation is based on the retrospective studies that showed that the majority of patients after acute GvHD develop chronic GvHD [21, 54]. The retrospective study by Inamoto et al. demonstrated that prolonging immunosuppressive therapy (IST) up to 18 months after transplantation was not associated with increased risk of a underlying disease relapse. The impact of prolonged IST on the subsequent risk and severity of chronic GvHD remains unknown [55]. The expert panel recommends not to prolong the IST beyond 12 months after HCT.

## Steroid-refractory acute GvHD

The results of the consensus are summarized in Table 2. The expert panel agreed that, if first-line therapy of acute GvHD included GCS, ruxolitinib should be the treatment of choice for both adults and children. This recommendation is based on the randomized REACH2 study [56]. If there is a response to second-line therapy, steroids should be the first drug to be discontinued, whereas the second-line medication to which the patient responded to, should be prolonged beyond GCS. This approach reflects the real-world practice with ruxolitinib where it was continued longer than GCS therapy [57-60]. The decision to use therapies other than ruxolitinib is made individually based on comorbidities, cytopenias, and emerging complications. In cases of grade 3 hematologic toxicity, the dose of ruxolitinib should be tapered by 50% and

**Table 2: Position statements for treatment of steroid-refractory acute GvHD**

| Position statement | % agreement | Category of recommendation |
|---|---|---|
| The drug of choice for the second-line therapy of acute GvHD, if the first-line therapy involved glucocorticosteroids, is ruxolitinib | 89% | 1 |
| In cases of grade 3 hematologic toxicity from ruxolitinib during the treatment of acute GvHD, its dose should be reduced by 50% | 71% | 1 |
| In cases of grade 4 hematologic toxicity from ruxolitinib during the treatment of acute GvHD, its dose should be reduced by 50% or therapy should be paused until neutrophil recovery above 500 cells/μL | 100% | 1 |
| In the third-line therapy of acute GvHD, combination therapy using methods for steroid-refractory GvHD is indicated | 90% | 2C |
| In the third-line therapy of acute GvHD, if ruxolitinib was used in the second line, the preferred methods are tumor necrosis factor antagonists or extracorporeal photopheresis | 100% | 2B |
| In addition to systemic therapy, fecal microbiota transplantation is indicated as the third-line therapy for intestinal form of acute GvHD | 81% | 2B |
| In the fourth-line therapy, a combination treatment is indicated | 100% | 2C |

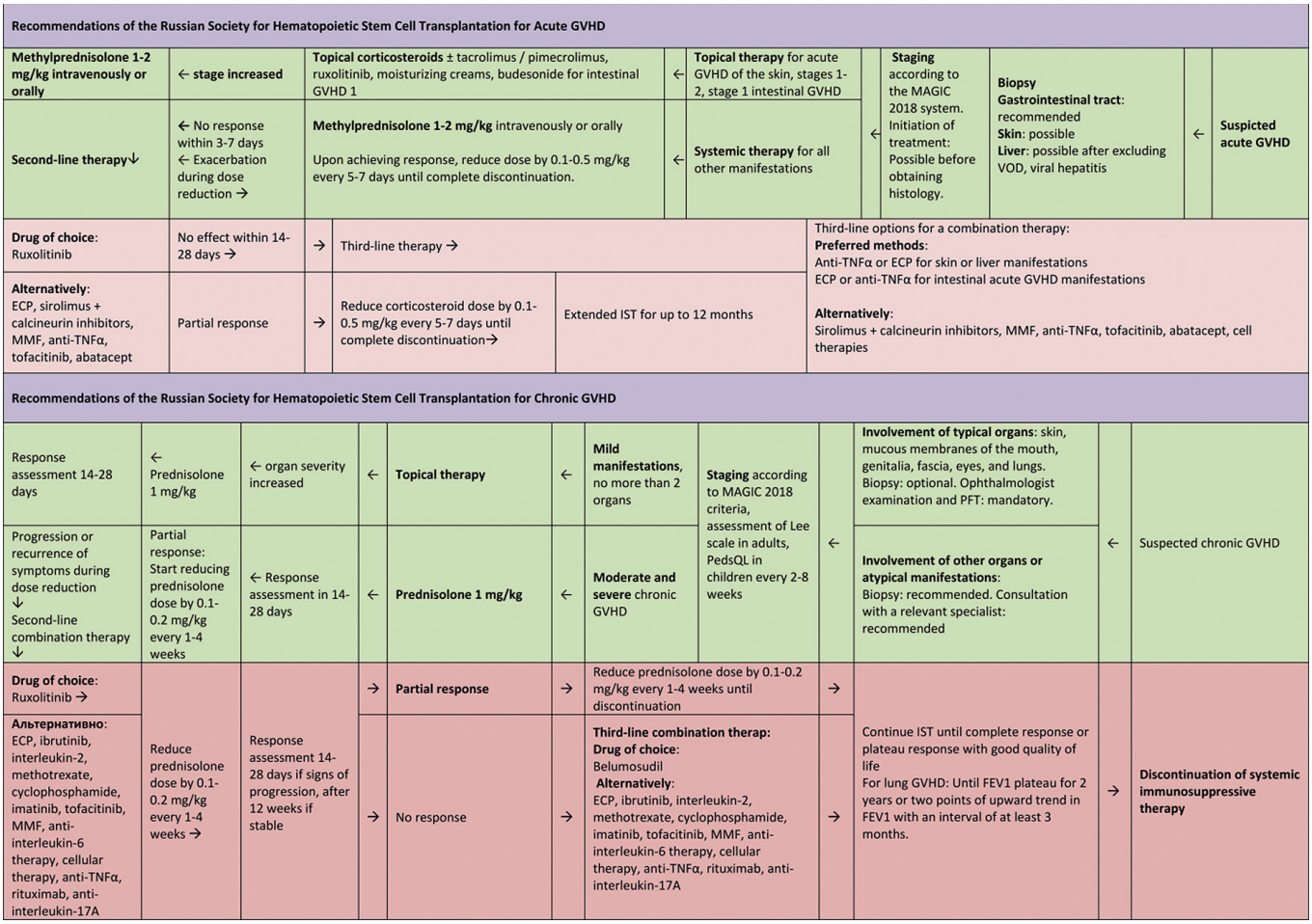


**Figure 1: Schematic presentation of major recommendations for acute GvHD therapies**

**Abbreviations used:** GvHD (graft-versus-host disease); GI tract (gastrointestinal tract); VOD (venoocclusive disease of a liver); ECP (extracorporeal photopheresis); anti-TNFα (tumor necrosis factor-alpha antagonists); CNI (calcineurin inhibitors); MMF (mycophenolate mofetil); FMT (fecal microbiota transplantation); PFT (pulmonary function test); GCs (glucocorticosteroids) FEV1 (forced expiratory volume in 1 second).

in case of grade 4 toxicity reduced by 50% or discontinued temporarily until resolution of the toxicity. These recommendations reflect partially the design of a registration study [56]. Alternatively, the experts mentioned extracorporeal photopheresis (ECP), tumor necrosis factor alpha antagonists (anti-TNFα), sirolimus in combination with calcineurin inhibitors, mycophenolate mofetil (MMF), tofacitinib and abatacept. All of these agents can be also considered in 3rd and subsequent lines of therapy. None of these treatment methods reached a consensus to be preferentially recommended. The rationale for a sequence of therapies after 2nd line and the need for combination approaches is not clearly defined by the published studies. Nonetheless, the consensus recommends using combination strategies in the 3rd and subsequent lines of acute GvHD therapy. Among the treatments recommended for 3rd and subsequent lines, anti-TNFα and ECP reached a sufficient agreement between the experts. The recommendation is based on several small studies demonstrating safety of combinations of these methods with ruxolitinib [61, 62, 63]. In ruxolitinib-refractory cases of acute GI GvHD, the expert panel recommends fecal microbiota transplantation (FMT) and anti-TNFα therapies. A number of prospective single center studies and a meta-analysis were published both in adults and children demonstrating the efficacy of this approach in the third-line therapy [64,68]. Simplified methods with *Bacteroides fragilis* PCR were proposed to assess microbiota engraftment [69]. The experts agreed that strategies incorporating combination treatments should be used after failure of a third-line therapy (Fig. 1).

## Diagnosis and treatment of chronic GvHD

The proposed position statements for chronic GvHD (cGvHD) diagnostics, evaluation and therapy are listed in Table 3.

The experts confirmed that National Institutes of Health (NIH) 2014 Consensus with 2018 EBMT-NIH-CIBMTR taskforce standardized terminology should be basic for chronic GvHD staging [11, 70]. This classification was validated in multiple prospective studies and predicts non-relapse mortality as well as the response to treatment [71-74]. Typical skin, oral, fascia, genital and lung chronic GvHD manifestations as *per* NIH 2017 were considered sufficient for a clinical diagnosis [11]. The expert panel recommended also inclusion of eye GvHD among the marker organs. The possible alternative etiologies of eye symptoms after HCT include allergic conjunctivitis, infectious uveitis or retinitis, comprising less than 5% of cases. All of these alternative conditions can be ruled out during the recommended ophthalmological examinations, including Schirmer's test, Ocular Surface Disease Index, cornea staining with fluorescein and conjunctival injection score. Sicca syndrome diagnosed by these diagnostic tools is a hallmark of chronic GvHD [75,76]. Diagnostic biopsy is recommended for atypical presentations, non-typical organ involvement and other suspected etiologies. In 2022 NIH consensus on atypical chronic GvHD was published stating that all previously described autoimmune diseases should be considered chronic GvHD manifestations. Especially in cases of sole atypical symptoms, biopsy of a target organ is recommended if it is applicable for this target organ [77]. Skin is the most commonly involved organ in chronic GvHD. Skin biopsy can be used to support the diagnosis or rule out alternative causes of skin manifestations. Punch biopsy is sufficient for non-sclerotic forms, and excision biopsy is required for sclerotic GvHD or fasciitis. In routine clinical practice skin biopsy is not performed often [78, 79]. Unlike acute GvHD and skin chronic GvHD, there is no consensus on pathological findings in lung biopsies. Therefore, the lung GvHD pathological diagnosis is based on comparison with previously published cases. The diagnosis of a lung GvHD should be made by a clinician and involve complex analysis of instrumental, clinical and laboratory findings [80-82]. As a consequence, the expert group has concluded that a biopsy may be beneficial for lung GvHD diagnosis, but is not mandatory in case of a typical chest tomography and FEV1/vital lung capacity (VLC) ratio with more significant FEV1 decline than that of VLC. The Lee Symptom Scale is an additional symptom assessment tool which was validated prospectively in several studies [83-85], also being used in randomized trial of ruxolitinib for steroid-refractory chronic GvHD [13]. The evidence for using PedsQL in children with GvHD is less robust, but this approach was still developed and validated [86].

The experts agreed that the goal of chronic GvHD treatment should be to decrease manifestations to mild in all involved organs with a good quality of life. No flares of chronic GvHD should be documented after treatment. This statement is based on the evidence that majority of patients with chronic GvHD cannot achieve a complete resolution of all symptoms within first five years after therapy initiation. On the contrary, more than half of the patients do achieve the abovementioned goal [87-89]. Mild manifestations of chronic GvHD do not lead to increased mortality [90], while quality of life with mild symptoms, according to NIH scale, were, generally, comparable with those in healthy population [91, 93]. Of course, the previous studies have shown that patients with severe disease were less likely to convert to mild manifestations [94-95]. However, the expert panel decided to promote further retrospective and prospective research, and faster switch to the novel effective treatment options in 3rd and subsequent lines in order to achieve chronic GvHD treatment goals in a larger proportion of patients.

Previous international consensuses established that minimal time of 1 month should be set for response assessment in chronic GvHD [20,94]. However, its progression can be detected earlier for certain features, like liver functional tests, oral involvement or skin changes. Thus, the expert group decided to keep the minimal time point of 14-28 days for assessing initial therapy of chronic GvHD, according to specific clinical presentation. For second-line therapy the minimal assessment time was set at 4 weeks according to the previous recommendations and studies [20, 90, 94]. In case of a stable disease, the recommended point for a switch of therapies is 12 weeks. The recommendation is based on Lee Symptom Scale assessment in the prospective randomized trial that demonstrated that a sufficient improvement in scores is observed not earlier than by 8 weeks, with more robust assessment at 12 weeks [95]. Overlap syndrome has a diverse clinical presentation, worse prognosis and worse response to both acute and chronic GvHD treatment protocols [96]. Thus, the expert group decided that, due to lack of well designed comparative studies, both acute and chronic GvHD treatment approaches can be used.

The experts agreed that mild chronic GvHD should be treated with topical therapy. A number of prospective studies

**Table 3: Position statements for diagnosis and treatment of chronic GvHD**

| Position statement | % agreement | Category of recommendation |
|---|---|---|
| Staging of chronic GvHD is performed according to the NIH 2017 criteria | 71% | 1 |
| Typical skin, oral, fascia, genitalia, lung and eye involvement may support clinical diagnosis, and do not require biopsy for confirmation | 88% | 2B |
| Skin biopsy is a clinical option to support a clinical diagnosis of chronic GvHD | 75% | 2B |
| In cases of a suspected lung GvHD with a typical chest tomography and FEV1/VLC ratio, lung biopsy is preferable, but not mandatory for an accurate diagnosis | 100% | 2B |
| In suspected chronic GvHD, biopsy of an involved organ may be performed in patients with atypical manifestations, absence of typical organ involvement or another suspected etiology | 94% | 2B |
| When assessing the response to systemic therapy for severe chronic GvHD without improvement by the NIH scale, it is recommended to use the Lee GvHD Symptom Scale for patients over 12 years old and PedsQL for those under 12 years old | 88% | 1 |
| In the presence of multiple options for therapy of chronic GvHD, a decrease of manifestations to mild degree in all involved organs with good quality of life is considered a sufficient response to systemic therapy | 93% | 2B |
| The minimum timeframe for making a decision on change of systemic therapy for chronic GvHD is 2-4 weeks, depending on the nature of clinical manifestations | 94% | 2C |
| The timeframe for deciding to change systemic therapy in the absence of progression of chronic GvHD is, at least, 4 weeks; in cases of satisfactory quality of life, the decision can be made after 12 weeks | 100% | 1 |
| When diagnosing an "overlap" syndrome of acute and chronic GvHD, treatment protocols for both acute and chronic GvHD may be used depending on the predominant clinical picture | 94% | 2B |
| Therapy for mild chronic GvHD should be conducted using topical treatments | 100% | 1 |
| Local therapy for chronic GvHD of a skin includes topical glucocorticosteroids or alternatively calcineurin inhibitors | 83% | 2B |
| Local therapy for chronic GvHD of the eyes includes artificial tears, dexamethasone and/or cyclosporine | 77% | 2B |
| Systemic therapy for chronic GvHD should be prescribed for moderate and severe clinical manifestations | 88% | 1 |
| In systemic treatment of chronic GvHD, it is advisable to re-initiate or continue "baseline" immunosuppressive therapy with calcineurin inhibitors, mTOR inhibitors, or ruxolitinib | 94% | 1 |
| Prednisolone (1 mg/kg) is the drug of choice for systemic glucocorticosteroid therapy in chronic GvHD | 82% | 1 |
| Initial therapy for chronic GvHD may be administered orally | 94% | 1 |
| The dose of glucocorticosteroids in the first-line therapy for chronic GvHD remains unchanged for the first 14-28 days | 100% | 2C |
| The recommended step for reducing glucocorticosteroid dose in the first-line therapy for chronic GvHD is individualized and ranges from 0.1 to 0.2 mg/kg | 100% | 2C |
| For atypical steroid-refractory forms of GvHD, the choice of therapy is made individually after consultation with a specialist | 71% | 2C |
| In cases of inefficacy of first-line glucocorticosteroid therapy for chronic GvHD and the addition of second-line therapy, a reduction in glucocorticosteroid dose should be initiated | 71% | 2C |
| Symptomatic therapy for individual organ manifestations can be used to improve quality of life | 100% | 2C |
| Ruxolitinib is the method of choice for second-line systemic therapy in chronic GvHD | 94% | 1 |
| Ruxolitinib is a drug of choice of the steroid-refractory lung chronic GvHD | 77% | 2C |
| Combined treatment is indicated for the second-line therapy of chronic GvHD | 82% | 2C |
| Combined treatment is indicated for the third-line therapy of chronic GvHD | 88% | 2C |
| Belumosudil is recommended for the third-line therapy of chronic GvHD | 82% | 2A |
| The duration of 2$^{nd}$ and subsequent lines of therapy for chronic GvHD is defined by a continuous clinical improvement over time. Stepwise discontinuation of immunosuppressive therapies should be performed if a plateau of response is reached in presence of good quality of life | 94% | 2C |

demonstrated response to topical tacrolimus, steroids, pimecrolimus and ruxolitinib [97-101]. Most of dermatological studies also recommend adjuvant lubricants [44]. In the absence of comparative trials on topical steroids *versus* newer drugs, the experts recommended to use steroid creams and ointments as the starting agents, while other topical therapies may be added in case of suboptimal efficacy or adverse events. Artificial tears is a standard of care for dry-eye syndrome in chronic GvHD patients. However, GCS and cyclosporine were reported to additionally decrease the symptoms based on Schirmer's test [102-104]. Use of eye drops with CS should be time-limited due to the risk of adverse events. There is a significant body of evidence that platelet-rich plasma (PRP) is associated with significant improvement of symptoms [105-107], however, due to undetermined legal status of this therapy in Russia beyond academic clinical studies, the official recommendation for PRP was not included in this statement. Additional options are sclera lences [108] and silicone punctal plugs [109].

The need of administering systemic treatment for moderate and severe chronic GvHD was demonstrated in a study by Sullivan et al. (1981). If left untreated, it leads to 80% mortality within a year [110]. Since the early studies, prednisone (1 mg/kg) was a standard of therapy [111]. All subsequent approaches with combination treatments failed to improve outcomes [112-116]. Thus, prednisone at 1 mg/kg is recommended as the starting therapy both for adults and children. Also the experts recommend continue or resume calcineurin inhibitors, or mTOR inhibitors, unless there was a documented intolerability of these agents. The recommendation is based on a randomized trial by Koc et al. that demonstrated reduced incidence of avascular necrosis with baseline calcineurin inhibitors combined with prednisone compared to prednisone alone [117]. The majority of randomized studies in chronic GvHD were performed with oral prednisone formulation, which is recommended as a preferred starting option, if a patient can tolerate oral medications. When switching administration routes, intravenous and oral formulations should be converted at the dosage equivalent of 1:1 [112-116]. The GCS dose should be kept stable for 14-28 days. Reducing the minimal time for changing therapies in the first line is based on the consideration, that some target organs may be assessed earlier, like liver function tests and oral GvHD. Also the panel considered the inclusion criteria in REACH3 trial that also declared more rapid switch of a therapy than 1 month [13]. The rates of steroid taper in case of a response are not well described in the literature; the expert panel recommended dose reduction by 0.1-0.2 mg/kg every 1-4 weeks depending on achieved response, thus being in line with previous recommendations [118]. The efficacy of standard chronic GvHD treatment in atypical forms of chronic GvHD is not well described. Therefore, the experts recommend consulting of a specialist involved in the treatment of autoimmune diseases affecting a target organ (neurologist, nephrologist, rheumatologist etc.).

## Steroid-refractory chronic GvHD

The recommendations for steroid-refractory chronic GvHD are presented in table 3. The expert group agreed that, upon initiation of a second-line therapy, the steroid dose should be tapered irrespectively of a therapeutic response. Failure to effectively taper GCS dose should be seen as an indication for switching to a second-line therapy. The GCS dose tapering should be made according to the abovementioned recommendations for patients in clinical response. The experts agreed that ruxolitinib should be a preferred second-line therapy of chronic GvHD both in adults and children as based on a positive randomized clinical trial [13] and supportive real-world evidence [119-122]. The panel recommended that initial second-line therapy should include a combination of treatment methods. However, the number of reasonable combinations was not agreed on. This recommendation goes in line with a randomized trial confirming a positive impact of adding calcineurin inhibitors [117]. The experts were asked if certain organ lesions in chronic GvHD should receive other therapies except ruxolitinib, but no manifestations reached the required consent for its inclusion into these guidelines. A consensus was reached to recommend belumosudil as a third-line therapy. The recommendation is based on prospective ROCKStar study that showed high response rate and favorable safety profile with low numbers of grade 3-4 adverse events [123]. No alternative third-line treatment reached the predefined level of agreement to be recommended. Alternative therapies that may be used in a third line, mentioned by the experts, include ECP, ibrutinib, interleukin-2, methotrexate, cyclophosphamide, imatinib, tofacitinib, MMF, anti-IL6 therapies, cell therapies, anti-TNFα therapies, rituximab, ant-interleukin-17A therapy. There was no consensus on clinical situations when these alternative therapies should be administered. All experts agreed that third-line chronic GvHD therapies should be performed with a combination of treatment methods.

The expert panel defined the criteria for stepwise discontinuation of IST in chronic GvHD without complete response. This criterion is a plateau of a response within 6 months with good quality of life assessed by attending physician or validated questionnaires. The probability of improving a response over time was never assessed for the diversity of clinical treatment options. Thus, an appropriate recommendation is made based on experts' clinical experience (Fig. 1).

## Steroid-free treatment of acute and chronic GvHD

In the Russian multicenter observational study, 35% of acute GvHD patients and 48% of chronic GvHD patients did not receive first-line therapy with GCS due to certain prophylaxis regimens and research protocols [21]. Therefore, the consensus decided that the issues of steroid-free first-line treatments should be considered despite lack of data (Table 4). Current evidence of steroid-free treatment is limited to an EBMT survey which has revealed that 52% of reporting centers do use steroid-free first-line chronic GvHD treatment, at least, in a minor subpopulation of patients. Among the reasons to apply this mode of therapy, the centers mentioned infections, diabetes, severe osteoporosis, avascular osteonecrosis, myopathy, sarcopenia, poor performance status, obesity, metabolic syndrome and poorly controlled hypertension [126]. Another study has shown the efficiency of acute and chronic GvHD treatment without GCS after novel prophylaxis protocols, e.g., post-transplant cyclophosphamide (PTCY), and alpha/beta-depletion-based regimens. The study demonstrated a 47% response in acute GvHD and 80% in chronic form. In acute GvHD, clinical responses were mostly restricted to stage III skin GvHD, while in chronic GvHD the probability of a response was higher in moderate disease than in severe-grade

disorder. Most common steroid-free regimens included calcineurin inhibitors or ruxolitinib [127]. Another study of registry data reported the use of such therapies around 18%, without mentioning the details on their modalities, or results of treatment [128]. In the randomized trial performed by Pidala et al. in low-risk acute GvHD, as based on Minnesota system, tacrolimus and sirolimus were non-inferior to steroids and were associated with a lower hyperglycemia incidence, reduced grade 2 to 3 infections, decreased rates of immune suppression discontinuation and improved patient-reported quality of life [129]. Another study evaluated steroid-free rituximab in mild-to-severe chronic GvHD patients, with clinical response in 88% of cases, but 37% of the responders had a subsequent flare [130]. In a small series of 6 cases, acute GvHD grade II-III was treated with single-agent ruxolitinib because of infectious complications, mostly, due to severe sepsis. Three patients were reported to have a partial response, and 3 patients showed a complete response [131].

The expert panel agreed that first-line therapy for acute and chronic GvHD may be conducted without systemic glucocorticosteroids in certain clinical situations, though in a routine clinical practice first line CS should remain a standard of care. For acute GvHD, calcineurin inhibitors and mTOR inhibitors should be considered as the first line, if prophylaxis regimen did not include these classes of drugs. For all other patients, ruxolitinib should be used as the drug of choice for a steroid-free regimen. The experts did not agree if any other forms besides grade II acute GvHD can be considered for steroid-free regimens. In cases of GCS-free treatment failure, systemic steroids should be used as second-line therapy.

Concerning patients with chronic GvHD, the consensus agreed that steroid-free first line treatment lacks reliable evidence. Appropriate indications and options for this therapy are decided individually. If this individual decision is made to pursue a steroid-free regimen in patients without calcineurin inhibitors and mTOR inhibitors in their prophylaxis regimen, one of these two classes of drugs should be administered; for other patients, calcineurin/mTOR inhibitors or ruxolitinib can be considered. The panel did not agree on distinct co-morbidities or GvHD manifestations that might be indications for a steroid-free regimen. The only agreement achieved for the patients with single organ involvement in moderate chronic GvHD, or mild GvHD manifestations in several organs that may be considered for a steroid-free regimens.

## CONCLUSION

The consensus of Russian Bone Marrow Transplantation Society has summarized the existing evidence in diagnosis and treatment of acute and chronic GvHD. The consensus was formulated by pediatric and adult centers and is applicable for both children and adults. The consensus also gathered expert opinions on aspects of acute and chronic GvHD, which were not supported by published studies and guide many aspects of a real world clinical practice. The authors acknowledge that there are limitations of this position statement. First, it represents the current existing body of evidence and contemporary views within a clinical community. The recommendations should be updated and corrected upon emergence of new data. Second, many aspects of acute and chronic GvHD did not get sufficient support within the panel of experts, or were not considered for voting. In this respect, we recommend using other international recommendations for guiding the treatment strategies. Third, many recommendations are not supported by strong published evidence. Therefore, if local standard operating procedures are already developed and underwent external accreditation or validation, they can supersede the 2C or 2B level recommendations of this consensus. The authors emphasize that standardization of GvHD treatment and prevention strategies is complicated by numerous patient-specific factors, including underlying diagnosis, infections complications, toxicity profile, thus requiring personalized management approaches.

## CONFLICT OF INTEREST

IM: Honoraria from Novartis, Sanofi, J&J, CLS Bering, Generium, Pfizer, research funding from Novartis.

ZN: Honoraria from Pfizer. The other authors report no conflicts of interest.

**Table 4: Summary of the consensus statements on steroid-free treatment of acute and chronic GvHD**

| Position statement | % agreement | Category of recommendation |
|---|---|---|
| First-line therapy for acute GvHD can be conducted without systemic glucocorticosteroids in certain clinical situations | 94% | 2B |
| If GvHD prophylaxis was performed without calcineurin inhibitors and mTOR inhibitors, the first line of immunosuppressive therapy for grade 2 acute GvHD is chosen individually | 94% | 2C |
| First-line systemic immunosuppressive therapy can be conducted without glucocorticosteroids using ruxolitinib | 72% | 2C |
| Glucocorticosteroids are the drug of choice for the second-line therapy of acute GvHD, if the first-line therapy was free of glucocorticosteroids | 83% | 2C |
| Treatment of chronic GvHD without glucocorticosteroids lacks reliable evidence, and decisions on clinical indications and options for this therapy are made individually | 82% | 2C |
| First-line therapy for chronic GvHD without glucocorticosteroids can be conducted with ruxolitinib or calcineurin/mTOR inhibitors | 71% | 2C |
| In patients without baseline immunosuppression with calcineurin inhibitors and mTOR inhibitors at the onset of chronic GvHD, the first line of systemic therapy can be conducted without glucocorticosteroids if a single organ is involved at moderate severity, or several organs are affected with mild manifestation | 75% | 2C |

## REFERENCES


1. Passweg JR, Baldomero H, Atlija M, Kleovoulou I, Witaszek A, Alexander T, et al. The 2023 EBMT report on hematopoietic cell transplantation and cellular therapies. Increased use of allogeneic HCT for myeloid malignancies and of CAR-T at the expense of autologous HCT. Bone Marrow Transplant. 2025; 50(6):1023-1032. doi: 10.1038/s41409-025-02524-2
2. McCann S, Gale RP. A brief history of bone marrow transplantation. Adv Cell Gene Ther. 2018;1(1):e8. doi: 10.1002/acg2.8
3. Greinix HT, Eikema DJ, Koster L, et al. Improved outcome of patients with graft-versus-host disease after allogeneic hematopoietic cell transplantation for hematologic malignancies over time: an EBMT mega-file study. Haematologica. 2022;107(5):1054-1063. doi: 10.3324/haematol.2020.265769
4. Pulanić D, Peczynski C, Boreland W, Schroeder T, Kröger N, Peffault de Latour R. Chronic graft-versus-host disease after allogeneic hematopoietic stem cell transplantation over 30 years: a multicenter retrospective study by the Transplant Complications Working Party of EBMT. Bone Marrow Transplant. 2023;58(Suppl 1):P197. doi: 10.1038/s41409-023-02056-7
5. Passweg JR, Baldomero H, Chabannon C, Corbacioglu S, Rafael de la Cámara, Dolstra H, et al. Impact of the SARS-CoV-2 pandemic on hematopoietic cell transplantation and cellular therapies in Europe 2020: a report from the EBMT activity survey. Bone Marrow Transplant. 2022; 57(5):742-752. doi: 10.1038/s41409-022-01604-x
6. Parovichnikova EN, Kuzmina LA., Vasilyeva VA, Pokrovskaya OS, Drokov MYu, Lukyanova IA, et al. The time factor and the allogeneic hematopoietic stem cell transplantation in patients with acute myeloid leukemia. Russian Journal of Hematology and Transfusiology. 2024; 69(3): 276-284 (In Russian). doi: 10.35754/0234-5730-2024-69-3-276-284
7. Zubarovskaya LS, Moiseev IS, Vladovskaya MD, Mikhailova NB, Morozova EV, Bykova TA, et al. Trends in outcome of hematopoietic stem cell transplantation: 5000 transplantations and 30 years of single-center experience. Cancers. 2023;15(19):4758-4772. doi: 10.3390/cancers15194758
8. Maschan MA, Scorobogatova EV, Shelichova LN, Ba lashov DN, Blagonravova OL, Dolgopolov IS, et al. Hematopoietic stem cell transplantation in children in Russia: a brief overview of activity in 2015-2018. Pediatr Hematol Oncol Immunopathol. 2020;19(2):22-29. (In Russian). doi: 10.24287/1726-1708-2020-19-2-22-29
9. Jagasia MH, Greinix HT, Arora M, Williams KM, Wolff D, Cowen EW, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. Biol Blood Marrow Transplant. 2015;21(3):382-390. doi: 10.1016/j.bbmt.2014.12.025
10. DeFilipp Z, Couriel DR, Lazaryan A, Bhatt VR., Buxbaum NP, Alousi AM, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: III. The 2020 Treatment of Chronic GVHD Report. Transplant Cell Ther. 2021; 27(9): 729-737. doi:10.1016/j.jtct.2021.05.004
11. Schoemans HM, Lee SJ, Ferrara JL, Wolff D, Levine JE, Schultz KR, et al. EBMT-NIH-CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment. Bone Marrow Transplant. 2018; 53(11): 1401-1415. doi: 10.1038/s41409-018-0204-7
12. Zeiser R, von Bubnoff N, Butler J, Mohty M, Niederwieser D, Or R, et al. Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease. N Engl J Med. 2020; 382 (19):1800-1810 doi: 10.1056/NEJMoa191763
13. Zeiser R, Polverelli N, Ram R, Hashmi SK, Chakraverty R, Middeke JM, et al. Ruxolitinib for Glucocorticoid-Refractory Chronic Graft-versus-Host Disease. N Engl J Med. 2021;385(3):228-38 doi: 10.1056/NEJMoa2033122
14. Carpenter PA, Kang HJ, Yoo KH, Zecca M, Cho B, Lucchini G, et al. Ibrutinib Treatment of Pediatric Chronic Graft-versus-Host Disease: Primary Results from the Phase 1/2 iMAGINE Study. Transplant Cell Ther. 2022;28(11):771.e1-771.e10. doi: 10.1016/j.jtct.2022.08.021
15. Waller EK, Miklos D, Cutler C, Arora M, Jagasia MH, Pusic I, et al. Ibrutinib for Chronic Graft-versus-Host Disease After Failure of Prior Therapy: 1-Year Update of a Phase 1b/2 Study. Biol Blood Marrow Transplant. 2019;25(10):2002-2007. doi: 10.1016/j.bbmt.2019.06.023
16. Cutler C, Lee SJ, Arai S, Rotta M, Zoghi B, Lazaryan A, et al. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar Study. Blood. 2021;138(22):2278-2289. doi: 10.1182/blood.2021012021
17. Koreth J, Matsuoka K, Kim HT, McDonough SM, Bindra B, Alyea EP 3rd, et al. Interleukin-2 and regulatory T cells in graft-versus-host disease. N Engl J Med. 2011;365(22):2055-66. doi: 10.1056/NEJMoa1108188
18. Kitko CL, Arora M, DeFilipp Z, Zaid MA, Di Stasi A, Radojcic V, et al. Axatilimab for Chronic Graft-Versus-Host Disease After Failure of at Least Two Prior Systemic Therapies: Results of a Phase I/II Study. J Clin Oncol. 2023;41(10):1864-1875. doi: 10.1200/JCO.22.00958.
19. Wais V, Gantner A, Strauss K, Neagoie A, Weidt C, Schnell J, et al. Treatment of steroid-refractory acute/chronic graft versus host disease: A single-center real-world experience of ruxolitinib in combination with extracorporeal photopheresis in a high-risk population. Leuk Res. 2024;147:107611. doi: 10.1016/j.leukres.2024.107611
20. Penack O, Marchetti M, Aljurf M, Arat M, Bonifazi F, Duarte RF, et al. Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2024;11(2):e147-e159

21. Moiseev IS, Drokov MY, Motorin DV, Badaev RS, Petrova GD, Bykova TA, et al. Multicenter non-interventional retrospective study: prevalence, clinical characteristics and approaches to the treatment of acute and chronic graft-versus-host disease in the Russian Federation. Cell Ther Transplant 2023; 12(4): 11-23. doi: 10.18620/ctt-1866-8836-2023-12-4-11-23
22. Schmalz U, Spinler S, Ringbeck J. Lessons Learned from a Two-Round Delphi-based Scenario Study. MethodsX. 2020;8:101-179. doi: 10.1016/j.mex.2020.101179
23. Weischendorff S, Kamari-Kany N, Kielsen K, Ifversen M, Müller K. Diagnosing Acute Graft-Versus-Host Disease in Children Undergoing Hematopoietic Stem Cell Transplantation-Comparison of the Modified Glucksberg Criteria Versus the MAGIC Criteria. Pediatr Blood Cancer. 2025;72(3):e31502. doi: 10.1002/pbc.31502
24. Bayraktar E, Graf T, Ayuk FA, Beutel G, Penack O, Luft T, et al. Data-driven grading of acute graft-versus-host disease. Nat Commun. 2023;14(1):77-99. doi: 10.1038/s41467-023-43372-2
25. Zhou Y, Barnett MJ, Rivers JK. Clinical significance of skin biopsies in the diagnosis and management of graft-vs-host disease in early postallogeneic bone marrow transplantation. Arch Dermatol. 2000;136(6):717-21. doi: 10.1001/archderm.136.6.717
26. Heldal D, Brinch L, Evensen SA, Tjønnfjord GE, Aamodt G, Elgjo K, Sviland L. Skin biopsies for early diagnosis and prognosis of graft-versus-host disease in recipients of allogeneic stem cells from blood or bone marrow. Bone Marrow Transplant. 2004;34(4):345-50. doi: 10.1038/sj.bmt.1704568
27. Firoz BF, Lee SJ, Nghiem P, Qureshi AA. Role of skin biopsy to confirm suspected acute graft-vs-host disease: results of decision analysis. Arch Dermatol. 2006;142(2):175-82. doi: 10.1001/archderm.142.2.175
28. Kreisel W, Dahlberg M, Bertz H, Harder J, Potthoff K, Deibert P, et al. Endoscopic diagnosis of acute intestinal GVHD following allogeneic hematopoietic SCT: a retrospective analysis in 175 patients. Bone Marrow Transplant. 2012;47(3):430-8. doi: 10.1038/bmt.2011.137
29. Scott AP, Henden AH, Kennedy GA, Tey SK. PET assessment of acute gastrointestinal graft versus host disease. Bone Marrow Transplant. 2023;58(9):973-979. doi: 10.1038/s41409-023-02038-9
30. Wild D, Sung AD, Cardona D, Cirricione C, Sullivan K, Detweiler C, et al. The Diagnostic Yield of Site and Symptom-Based Biopsies for Acute Gastrointestinal Graft-Versus-Host Disease: A 5-Year Retrospective Review. Dig Dis Sci. 2016;61(3):806-13. doi: 10.1007/s10620-015-3938-8
31. Akahoshi Y, Kimura SI, Tada Y, Matsukawa T, Tamaki M, Doki N, et al. Cytomegalovirus gastroenteritis in patients with acute graft-versus-host disease. Blood Adv. 2022;6(2):574-584. doi: 10.1182/bloodadvances.2021005885
32. McDonald GB, Tabellini L, Storer BE, Lawler RL, Martin PJ, Hansen JA. Plasma biomarkers of acute GVHD and nonrelapse mortality: predictive value of measurements before GVHD onset and treatment. Blood. 2015;126(1):113-20. doi: 10.1182/blood-2015-03-636753
33. Paviglianiti A, Maia T, Gozlan JM, Brissot E, Malard F, Banet A, et al. Human herpesvirus type 6 reactivation after haploidentical hematopoietic cell transplantation with post-transplant cyclophosphamide and antithymocyte globulin: risk factors and clinical impact. Clin Hematol Int. 2024;6(1):26-38. doi: 10.46989/001c.92525
34. Neuberger J, Patel J, Caldwell H, Davies S, Hebditch V, Hollywood C, et al. Guidelines on the use of liver biopsy in clinical practice from the British Society of Gastroenterology, the Royal College of Radiologists and the Royal College of Pathology. Gut. 2020;69(8):1382-1403. doi: 10.1136/gutjnl-2020-321299
35. Stueck AE, Schiano TD, Fiel MI. Development of a novel histologic diagnostic algorithm for hepatic graft-versus-host disease. Modern Pathology. 2018; 31(3): 442-451. doi: 10.1038/modpathol.2017.151
36. Bacigalupo A, Milone G, Cupri A, Severino A, Fagioli F, Berger M, et al. Steroid treatment of acute graft-versus-host disease grade I: a randomized trial. Haematologica. 2017;102(12):2125-2133. doi: 10.3324/haematol.2017.171157
37. Elad S, Or R, Resnick I, Shapira MY. Topical tacrolimus--a novel treatment alternative for cutaneous chronic graft-versus-host disease. Transpl Int. 2003 Sep;16(9):665-70. doi: 10.1007/s00147-003-0594-2.
38. Choi CJ, Nghiem P. Tacrolimus ointment in the treatment of chronic cutaneous graft-vs-host disease: a case series of 18 patients. Arch Dermatol. 2001 Sep;137(9):1202-6. doi: 10.1001/archderm.137.9.1202
39. Frairia C, Nicolosi M, Shapiro J, Kim J, Betts BC, Fernandez HF, et al. Sole Upfront Therapy with Beclomethasone and Budesonide for Upper Gastrointestinal Acute Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2020;26(7):1303-1311. doi: 10.1016/j.bbmt.2020.04.023
40. Cook M, Vadakkel G, Chinapen S, Perales MA; Tamari R, Papadopoulos EB, et al. Efficacy of Budesonide Monotherapy for Low Grade GI Gvhd after Post Transplant Cyclophosphamide. Blood. 2024; 144: 7356-7357. doi: 10.1182/blood-2024-200361
41. Hockenbery DM, Cruickshank S, Rodell TC, Gooley T, Schuening F, Rowleyet S, et al. A randomized, placebo-controlled trial of oral beclomethasone dipropionate as a prednisone-sparing therapy for gastrointestinal graft-versus-host disease. Blood. 2007; 109(10): 4557-63. doi: 10.1182/blood-2006-05-021139
42. McDonald GB, Bouvier M, Hockenbery DM, Stern JM, Gooley T, Farrand A, et al. Oral beclomethasone dipropionate for treatment of intestinal graft-versus-host disease: a randomized, controlled trial. Gastroenterology. 1998; 115(1): 28-35. doi: 10.1016/s0016-5085(98)70361-0
43. Couriel D, Carpenter PA, Cutler C, Bolaños J, Treister NS, Gea-Banacloche J, et al. Ancillary therapy and supportive care of chronic graft-versus-host disease: National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: V. Ancillary therapy and supportive care working group report. Biol Blood Marrow Transplant 2006; 12(4):375-96. doi: 10.1016/j.bbmt.2006.02.003

44. Marks C, Stadler M, Häusermann P, Wolff D, Buchholz S, Stary G, et al. German-Austrian-Swiss Consensus Conference on clinical practice in chronic graft-versus-host disease (GVHD): guidance for supportive therapy of chronic cutaneous and musculoskeletal GVHD. Br J Dermatol. 2011;165(1):18-29. doi: 10.1111/j.1365-2133.2011.10360.x
45. Schmook T, Kraft J, Benninghoff B, Nindl I, Roewert J, Ulrich C, Stockfleth E. Treatment of cutaneous chronic graft-versus-host disease with topical pimecrolimus. Bone Marrow Transplant. 2005; 36(1):87-88. doi: 10.1038/sj.bmt.1704998
46. Hudda Z, Flannery A, Teusink-Cross A, Davies SM, Khandelwal P, et al. Topical ruxolitinib is promising as sole or adjunctive therapy in treating maculopapular rash of acute and chronic skin GVHD. Bone Marrow Transplant. 2024; 59(3):425-427. doi: 10.1038/s41409-023-02181-3
47. Van Lint MT, Uderzo C, Locasciulli A, Majolino I, Scimé R, Locatelli F, et al. Early treatment of acute graft-versus-host disease with high- or low-dose 6-methylprednisolone: a multicenter randomized trial from the Italian Group for Bone Marrow Transplantation. Blood. 1998;92(7):2288-93.
48. Martin PJ, Rizzo JD, Wingard JR, Ballen K, Curtin PT, Cutler C, et al. First- and second-line systemic treatment of acute graft-versus-host disease: recommendations of the American Society of Blood and Marrow Transplantation. Biol Blood Marrow Transplant. 2012;18(8):1150-63. doi: 10.1016/j.bbmt.2012.04.005
49. Mielcarek M, Storer BE, Boeckh M, Carpenter PA, McDonald GB, Deeg HJ, et al. Initial therapy of acute graft-versus-host disease with low-dose prednisone does not compromise patient outcomes. Blood. 2009;113(13):2888-94. doi: 10.1182/blood-2008-07-168401
50. Westin JR, Saliba RM, De Lima M, Alousi A, Hosing C, Qazilbash MH, et al. Steroid-Refractory Acute GVHD: Predictors and Outcomes. Adv Hematol. 2011;2011(1):601953. doi: 10.1155/2011/601953
51. Kanakry CG, Bolaños-Meade J, Kasamon YL, Zahurak M, Durakovic N, Furlong T, et al. Low immunosuppressive burden after HLA-matched related or unrelated BMT using posttransplantation cyclophosphamide. Blood. 2017;129(10):1389-1393. doi: 10.1182/blood-2016-09-737825
52. Shelikhova L, Ilushina M, Shekhovtsova Z, Shasheleva D, Khismatullina R, Kurnikova E, et al. αβ T Cell-Depleted Haploidentical Hematopoietic Stem Cell Transplantation without Antithymocyte Globulin in Children with Chemorefractory Acute Myelogenous Leukemia. Biol Blood Marrow Transplant. 2019;25(5):e179-e182. doi: 10.1016/j.bbmt.2019.01.023
53. Akahoshi Y, Spyrou N, Hoepting M, Aguayo-Hiraldo P, Ayuk F, Chanswangphuwana C, et al. Flares of acute graft-versus-host disease: a Mount Sinai Acute GVHD International Consortium analysis. Blood Adv. 2024;8(8):2047-2057. doi: 10.1182/bloodadvances. 2023012091
54. Inamoto Y, Martin PJ, Storer BE, Mielcarek M, Storb RF, Carpenter PA. Response endpoints and failure-free survival after initial treatment for acute graft-versus-host disease. Haematologica. 2014; 99(2):385-391. doi: 10.3324/haematol. 2013.093062
55. Inamoto Y, Flowers ME, Lee SJ, Carpenter PA, Warren EH, Deeg HJ et al. Influence of immunosuppressive treatment on risk of recurrent malignancy after allogeneic hematopoietic cell transplantation. Blood. 2011;118(2):456-63. doi: 10.1182/blood-2011-01-330217
56. Zeiser R, von Bubnoff N, Butler J, Mohty M, Niederwieser D, Or R, et al. Ruxolitinib for Glucocorticoid-Refractory Acute Graft-versus-Host Disease. N Engl J Med. 2020; 382(19):1800-1810. doi: 10.1056/NEJMoa1917635
57. Moiseev IS, Morozova EV, Bykova TA, Paina OV, Smirnova AG, Dotsenko AA, et al. Long-term outcomes of ruxolitinib therapy in steroid-refractory graft-versus-host disease in children and adults. Bone Marrow Transplant. 2020;55(7):1379-1387. doi: 10.1038/s41409-020-0834-4
58. Escamilla V, García-Gutiérrez V, López Corral L, García Cadenas I, Pérez Martínez A, Márquez Malaver FJ, et al. Ruxolitinib in refractory acute and chronic graft-versus-host disease: a multicenter survey study. Bone Marrow Transplant. 2020;55(3):641-648. doi: 10.1038/s41409-019-0731-x
59. Uygun V, Karasu G, Daloğlu H, Öztürkmen S, Çakı Kılıç S, Yalçın K, et al. Ruxolitinib salvage therapy is effective for steroid-refractory graft-versus-host disease in children: A single-center experience. Pediatr Blood Cancer. 2020;67(4):e28190. doi: 10.1002/pbc.28190
60. Dang SH, Liu Q, Xie R, Shen N, Zhou S, Shi W, Liu W, Zou P, You Y, Zhong ZD. Ruxolitinib add-on in corticosteroid-refractory graft-vs-host disease after allogeneic stem cell transplantation: Results from a retrospective study on 38 Chinese patients. World J Clin Cases. 2020;8(6):1002-1187.
61. Zhao Y, Wu H, Shi J, Luo Y, Li X, Lan J, et al. Ruxolitinib combined with etanercept induce a rapid response to corticosteroid-refractory severe acute graft vs host disease after allogeneic stem cell transplantation: Results of a multi-center prospective study. Am J Hematol. 2020;95(9):1075-1084. doi: 10.1002/ajh.25898
62. Modemann F, Ayuk F, Wolschke C, Christopeit M, Janson D, von Pein UM, Kröger N. Ruxolitinib plus extracorporeal photopheresis (ECP) for steroid refractory acute graft-versus-host disease of lower GI-tract after allogeneic stem cell transplantation leads to increased regulatory T cell level. Bone Marrow Transplant. 2020;55(12):2286-2293. doi: 10.1038/s41409-020-0952-z
63. Wais V, Gantner A, Strauss K, Neagoie A, Weidt C, Schnell J, Döhner H, Bunjes D, Sala E. Treatment of steroid-refractory acute/chronic graft versus host disease: A single-center real-world experience of ruxolitinib in combination with extracorporeal photopheresis in a high-risk population. Leuk Res. 2024;147:107611. doi: 10.1016/j.leukres.2024.107611
64. Goeser F, Sifft B, Stein-Thoeringer C, Farowski F, Strassburg CP, Brossart P, et al. Fecal microbiota transfer for refractory intestinal graft-versus-host disease – Experience from two German tertiary centers. Eur J Haematol. 2021;107(2):229-245. doi: 10.1111/ejh.13642

65. van Lier YF, Davids M, Haverkate NJE, de Groot PF, Donker ML, Meijer E, et al. Donor fecal microbiota transplantation ameliorates intestinal graft-versus-host disease in allogeneic hematopoietic cell transplant recipients. Sci Transl Med. 2020; 12(556):eaaz8926. doi: 10.1126/scitranslmed.aaz8926

66. Goloshchapov OV, Chukhlovin AB, Stanevich OV, Klement'eva RV, Shcherbakov AA, Shvetsov AN, et al. Fecal microbiota transplantation in children: first experience and prospects for clinical application. Pediatria. 2021; 100 (3): 17-27 (In Russian). doi: 10.24110/0031-403X-2021-100-3-17-27

67. Qi X, Li X, Zhao Y, Wu X, Chen F, Ma X, Zhang F, Wu D. Treating Steroid Refractory Intestinal Acute Graft-vs.-Host Disease With Fecal Microbiota Transplantation: A Pilot Study. Front Immunol. 2018;9:2195. doi: 10.3389/fimmu.2018.02195

68. Biliński J, Jasiński M, Basak GW. The Role of Fecal Microbiota Transplantation in the Treatment of Acute Graft-versus-Host Disease. Biomedicines. 2022;10(4):837. doi: 10.3390/biomedicines10040837

69. Goloshchapov OV, Bakin EA, Kucher MA, Stanevich OV, Suvorova MA, Gostev VV, et al. Bacteroides fragilis is a potential marker of effective microbiota transplantation in acute graft-versus-host disease treatment. Cell Ther Transplant. 2020; 9 (2), 47-59. doi: 10.18620/ctt-1866-8836-2020-9-2-47-59

70. Pavletic SZ, Vogelsang GB, Lee SJ. 2014 National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: preface to the series. Biol Blood Marrow Transplant. 2015;21(3):387-388. doi: 10.1016/j.bbmt.2014.12.035

71. Aisa Y, Mori T, Kato J, Yamane A, Kohashi S, Kikuchi T, Okamoto S, et al. Validation of NIH consensus criteria for diagnosis and severity-grading of chronic graft-versus-host disease. Int J Hematol. 2013;97(2):263-271. doi: 10.1007/s12185-013-1268-1

72. Inamoto Y, Chai X, Kurland BF, Cutler C, Flowers ME, Palmer JM, et al. Validation of measurement scales in ocular graft-versus-host disease. Ophthalmology. 2012;119(3):487-493. doi: 10.1016/j.ophtha.2011.08.040

73. Moon JH, Sohn SK, Lambie A, Ellis L, Hamad N, Uhm J, et al. Validation of National Institutes of Health global scoring system for chronic graft-versus-host disease (GVHD) according to overall and GVHD-specific survival. Biol Blood Marrow Transplant. 2014;20(4):556-63. doi: 10.1016/j.bbmt.2014.01.010

74. Lee SJ, Wolff D, Kitko C, Koreth J, Inamoto Y, Jagasia M, et al. Measuring therapeutic response in chronic graft-versus-host disease. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: IV. The 2014 Response Criteria Working Group report. Biol Blood Marrow Transplant. 2015;21(6):984-99. doi: 10.1016/j.bbmt.2015.02.025

75. Ogawa Y, Kim SK, Dana R, Clayton J, Jain S, Rosenblatt MI, et al. International Chronic Ocular Graft-vs-Host-Disease (GVHD) Consensus Group:Proposed diagnostic criteria for chronic GVHD (Part I) Sci Rep. 2013;3:3419. doi: 10.1038/srep03419

76. Nassar A, Tabbara KF, Aljurf M. Ocular manifestations of graft-versus-host disease. Saudi J Ophthalmol. 2013;27(3):215-22. doi: 10.1016/j.sjopt.2013.06.007

77. Cuvelier GDE, Schoettler M, Buxbaum NP, Pinal-Fernandez I, Schmalzing M, Distler JHW, et al. Toward a Better Understanding of the Atypical Features of Chronic Graft-Versus-Host Disease: A Report from the 2020 National Institutes of Health Consensus Project Task Force. Transplant Cell Ther. 2022;28(8):426-445. doi: 10.1016/j.jtct.2022.05.038

78. Hillen U, Häusermann P, Massi D, Janin A, Wolff D, Lawitschka A, et al. Histopathologic Diagnosis of Chronic Graft-versus-Host Disease: National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: II. Pathology Working Group Report. Biol Blood Marrow Transplant. 2006;12(1):31-47. doi: 10.1016/j.bbmt.2005.10.023

79. Hillen U, Häusermann P, Massi D, Janin A, Wolff D, Lawitschka A, Greinix H, Meyer R, Ziemer M. Consensus on performing skin biopsies, laboratory workup, evaluation of tissue samples and reporting of the results in patients with suspected cutaneous graft-versus-host disease. 2015;29(5):948-54. doi: 10.1111/jdv.12737

80. Archer G, Berger I, Bondeelle L, de Margerie-Mellon C, Cassonnet S, Peffault de Latour R, et al. Interstitial lung diseases after hematopoietic stem cell transplantation: New pattern of lung chronic graft-versus-host disease? Bone Marrow Transplant. 2023; 58(1), 87-93 (2023). doi: 10.1038/s41409-022-01859-4

81. Yousem SA. The histological spectrum of pulmonary graft-versus-host disease in bone marrow transplant recipients. Hum Pathol. 1995;26(6):668-75. doi: 10.1016/0046-8177(95)90174-4

82. Shulman HM, Kleiner D, Lee SJ, Morton T, Pavletic SZ, Farmer E, et al. Histopathologic Diagnosis of Chronic Graft-versus-Host Disease: National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: II. Pathology Working Group Report. Biol Blood Marrow Transplant. 2006;12(1):31-47. doi: 10.1016/j.bbmt.2005.10.023

83. Lee S, Cook EF, Soiffer R, Antin JH. Development and validation of a scale to measure symptoms of chronic graft-versus-host disease. Biol Blood Marrow Transplant. 2002; 8(8):444-452. doi: 10.1053/bbmt.2002.v8.pm12234170

84. Merkel EC, Mitchell SA, Lee SJ. Content validity of the Lee Chronic Graft-versus-Host Disease Symptom Scale as assessed by cognitive interviews. Biol Blood Marrow Transplant. 2016;22(4):752-758. doi: 10.1016/j.bbmt.2015.12.026

85. Vasconcellos de Souza C, Vigorito AC, Miranda ECM, Garcia Jr C, Colturato VAR, Mauad M, et al. Translation, cross-cultural adaptation, and validation of the Lee Chronic Graft-versus-Host Disease Symptom Scale in a Brazilian population. Biol Blood Marrow Transplant. 2016;22(7):1313-1318. doi: 10.1016/j.bbmt.2016.03.013

86. Lawitschka A, Güclü ED, Varni JW, Putz M, Wolff D, Pavletic S, Greinix H, Peters C, Felder-Puig R. Health-related quality of life in pediatric patients after allogeneic SCT: development of the PedsQL Stem Cell Transplant module and results of a pilot study. Bone Marrow Transplant. 2014;49(8):1093-7. doi: 10.1038/bmt.2014.96

87. Lee SJ, Nguyen TD, Onstad L, Bar M, Krakow EF, Salit RB, et al. Success of Immunosuppressive Treatments in Patients with Chronic Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2018;24(3):555-562. doi: 10.1016/j.bbmt.2017.10.042

88. Moiseev IS, Dotsenko AA, Smirnova AG, Vlasova Y.Y., Morozova EV, et al. Long-term goals in the treatment of chronic graft-versus-host disease after matched allogeneic hematopoietic stem cell transplantation. Cell Ther Transplant. 2020;9(4):29-36. doi: 10.18620/ctt-1866-8836-2020-9-4-29-36

89. Bacigalupo A, Sica S, van Lint MT. Failure to effectively treat chronic graft-versus-host disease: a strong call for prevention. Haematologica. 2016;101(5):e214-5. doi: 10.3324/haematol.2015.138040

90. Martin PJ, Storer BE, Inamoto Y, Flowers MED, Carpenter PA, et al. An endpoint associated with clinical benefit after initial treatment of chronic graft-versus-host disease. Blood. 2017;130(3):360-367. doi: 10.1182/blood-2017-03-775767

91. Fiuza-Luces C, Simpson RJ, Ramírez M, Lucia A, Berger NA. Physical function and quality of life in patients with chronic GvHD: a summary of preclinical and clinical studies and a call for exercise intervention trials in patients. Bone Marrow Transplant. 2016;51(1):13-26. doi: 10.1038/bmt.2015.195

92. Fiuza-Luces C, Simpson RJ, Ramírez M, Lucia A, Berger NA. Physical function and quality of life in patients with chronic GvHD: a summary of preclinical and clinical studies and a call for exercise intervention trials in patients. Bone Marrow Transplant. 2016;51(1):13-26. doi: 10.1038/bmt.2015.195

93. Obidoa CA, Reisine SL, Cherniack M. How does the SF-36 perform in healthy populations? A structured review of longitudinal studies. J Soc Behav Health Sci. 2010;4(1):30-48. doi: 10.5590/JSBHS.2010.04.1.02

94. Martin PJ, Inamoto Y, Carpenter PA, Lee SJ, Flowers ME. Treatment of chronic graft-versus-host disease: Past, present and future. Korean J Hematol. 2011;46(3):153-63. doi: 10.5045/kjh.2011.46.3.153

95. Lee S, Locatelli F, Ayuk FA, Zuckerman T, Fukushima K, Vallejo Llamas JC, et al. Patient-Reported Outcomes (PROs) Among Patients With Steroid-Refractory or -Dependent Chronic Graft-vs-Host Disease (cGVHD) Randomized to Ruxolitinib (RUX) vs Best Available Therapy (BAT). Blood. 2021; 138: 3909-3911. doi: 10.1182/blood-2021-144576

96. Pidala J, Vogelsang G, Martin P, Chai X, Storer B, Pavletic S, et al. Overlap subtype of chronic graft-versus-host disease is associated with an adverse prognosis, functional impairment, and inferior patient-reported outcomes: a Chronic Graft-versus-Host Disease Consortium study. Haematologica. 2012;97(3):451-8. doi: 10.3324/haematol.2011.055186

97. Markova A, Papadopoulos EB, Dusza S, Perales MA, Harris AC, Ponce DM, et al. Phase 2 Trial of Ruxolitinib Cream for Chronic Cutaneous GvHD. Transplant Cell Ther. 2024; 30(2S):S1-5. doi: 10.1016/j.jtct.2023.12.019

98. Choi CJ, Nghiem P. Tacrolimus ointment in the treatment of chronic cutaneous graft-vs-host disease: a case series of 18 patients. Arch Dermatol. 2001;137(9):1202–1206. doi: 10.1001/archderm.137.9.1202

99. Ziemer M, Gruhn B, Thiele JJ, Elsner P. Treatment of extensive chronic cutaneous graft-versus-host disease in a infant with topical pimecrolimus. J Am Acad Dermatol. 2004;50(6):946-948. doi: 10.1016/j.jaad.2004.02.010

100. Hymes SR, Alousi AM, Cowen EW. Graft-versus-host disease: part II. Management of cutaneous graft-versus-host disease. J Am Acad Dermatol. 2012;66(4):535.e1-535.e16. doi: 10.1016/j.jaad.2011.11.961

101. Carpenter PA, Kitko CL, Elad S, Flowers ME, Gea-Banacloche JC, Halter JP, et al. National Institutes of Health Consensus Development Project on criteria for clinical trials in chronic graft-versus-host disease: V. The 2014 Ancillary Therapy and Supportive Care Working Group report. Biol Blood Marrow Transplant. 2015;21(7):1167-1187. doi: 10.1016/j.bbmt.2015.03.024

102. Yin J, Kheirkhah A, Dohlman T, Saboo U, Dana R. Reduced Efficacy of Low-dose Topical Steroids in Dry Eye Disease Associated With Graft-versus-Host Disease. Am J Ophthalmol. 2018;190:17-23. doi: 10.1016/j.ajo.2018.03.024

103. Lelli GJ Jr, Musch DC, Gupta A, Farjo QA, Nairus TM, Mian SI. Ophthalmic cyclosporine use in ocular GVHD. Cornea. 2006;25(6):635-8. doi: 10.1097/01.ico.0000208818.47861.1d

104. Yalçindağ N, Bingöl Kiziltunç P, Çelik T, Ertem M, İnce E, Atilla H. Topical cyclosporine-A in pediatric ocular graft versus host disease. AAPOS. 2018; 22(4): e84-e85. doi: 10.1016/j.jaapos.2018.07.311

105. Pezzotta S, Del Fante C, Scudeller L, Cervio M, Antoniazzi ER, Perotti C. Autologous platelet lysate for treatment of refractory ocular GVHD. Bone Marrow Transplant. 2012;47(12):1558-63. doi: 10.1038/bmt.2012.64

106. Mancini M, Postorino EI, Gargiulo L, Aragona P. Use of allogeneic platelet-rich plasma for the treatment of autoimmune ocular surface disorders: case series. Front. Ophthalmol. 2023; 3: 1215848. doi: 10.3389/fopht.2023.1215848

107. Ronci C, Ferraro AS, Lanti A, Missiroli F, Sinopoli S, Del Proposto G, et al. Platelet-rich plasma as treatment for persistent ocular epithelial defects. Transfus Apher Sci. 2015;52(3):300-4. doi: 10.1016/j.transci.2014.12.027

108. Bligdon SM, Colarusso BA, Ganjei AY, Kwok A, Luo ZK, Brocks D. Scleral Lens and Prosthetic Replacement of the Ocular Surface Ecosystem Utilization in Ocular Graft-versus-Host Disease: A Survey Study. Clin Ophthalmol. 2021 Dec 25;15:4829-4838. doi: 10.2147/OPTH.S337824

109. Singh RB, Yung A, Coco G, Sinha S, Dohlman TH et al. Efficacy and retention of silicone punctal plugs for treatment of dry eye in patients with and without ocular graft-versus-host-disease. Ocul Surf. 2020 Oct;18(4):731-735. doi: 10.1016/j.jtos.2020.07.018. Epub 2020 Jul 30.

110. Sullivan KM, Shulman HM, Storb R, Weiden PL, Witherspoon RP, McDonald GB et al. Chronic graft-versus-host disease in 52 patients: adverse natural course and successful treatment with combination immunosuppression. Blood. 1981; 57(2):267-276. doi: 10.1182/blood.V57.2.267.267

111. Sullivan KM, Witherspoon RP, Storb R, Deeg HJ, Dahlberg S, Sanders JE, Appelbaum FR, et al. Alternating-day cyclosporine and prednisone for treatment of high-risk chronic graft-v-host disease. Blood. 1988; 72(2):555-561. doi: 10.1182/blood.V72.2.555.555

112. Cragg L, Blazar BR, Defor T, Kolatker N, Miller W, Kersey J, Ramsay M, McGlave P, Filipovich A, Weisdorf D. A randomized trial comparing prednisone with antithymocyte globulin/prednisone as an initial systemic therapy for moderately severe acute graft-versus-host disease. Biol Blood Marrow Transplant. 2000;6(4A):441-7. doi: 10.1016/s1083-8791(00)70036-x

113. Alousi AMA, Weisdorf DJ, Logan BR, Bolaños-Meade J, Carter S, Difronzo N, et al. Etanercept, mycophenolate, denileukin, or pentostatin plus corticosteroids for acute graft-versus-host disease: a randomized phase 2 trial from the Blood and Marrow Transplant Clinical Trials Network. Blood. 2009;114(3):511-7. doi: 10.1182/blood-2009-03-212290

114. Lee SJ, Zahrieh D, Agura E, MacMillan ML, Maziarz RT, McCarthy PL Jr, et al. Effect of up-front daclizumab when combined with steroids for the treatment of acute graft-versus-host disease: results of a randomized trial. Blood. 2004;104(5):1559-64. doi: 10.1182/blood-2004-03-0854

115. Bolaños-Meade J, Logan BR, Alousi AM, Antin JH, Barowski K, Carter SL, et al. Phase 3 clinical trial of steroids/mycophenolate mofetil vs steroids/placebo as therapy for acute GVHD: BMT CTN 0802. Blood. 2014; 124(22):3221-7. doi: 10.1182/blood-2014-06-577023

116. Mielcarek M, Storer BE, Boeckh M, Carpenter PA, McDonald GB, Deeg HJ, et al. Initial therapy of acute graft-versus-host disease with low-dose prednisone does not compromise patient outcomes. Blood. 2009; 113(13): 2888-2894. doi: 10.1182/blood-2008-07-168401

117. Koc S, Leisenring W, Flowers ME, Anasetti C, Deeg HJ, Nash RA, et al. Therapy for chronic graft-versus-host disease: a randomized trial comparing cyclosporine plus prednisone versus prednisone alone. Blood. 2002;100(1):48-51. doi: 10.1182/blood.v100.1.48.

118. Vogelsang GB. How I treat chronic graft-versus-host disease. Blood. 2001; 97 (5): 1196-1201. doi: 10.1182/blood.v97.5.1196

119. Modi B, Hernandez-Henderson M, Yang D, Klein J, Dadwal S, Kopp E, et al. Ruxolitinib as Salvage Therapy for Chronic Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2019;25(2):265-269. doi: 10.1016/j.bbmt.2018.09.003

120. González Vicent M, Molina B, González de Pablo J, Castillo A, Díaz MÁ. Ruxolitinib treatment for steroid refractory acute and chronic graft vs host disease in children: Clinical and immunological results. Am J Hematol. 2019;94(3):319-326. doi: 10.1002/ajh.25376

121. Escamilla Gómez V, García-Gutiérrez V, López Corral L, García Cadenas I, Pérez Martínez A, Márquez Malaver FJ, et al. Ruxolitinib in refractory acute and chronic graft-versus-host disease: a multicenter survey study. Bone Marrow Transplant. 2020;55(3):641-648. doi: 10.1038/s41409-019-0731-x

122. Baccelli F, Gottardi F, Muratore E, Leardini D, Grasso AG, Gori D, et al. Ruxolitinib for the treatment of acute and chronic graft-versus-host disease in children: a systematic review and individual patient data meta-analysis. Bone Marrow Transplant. 2024;59(6):765-776. doi: 10.1038/s41409-024-02252-z

123. Cutler C, Lee SJ, Arai S, Rotta M, Zoghi B, Lazaryan A, et al. Belumosudil for chronic graft-versus-host disease after 2 or more prior lines of therapy: the ROCKstar study. Blood. 2021;138(22):2278-2289. doi: 10.1182/blood.2022015598

124. Pidala J, Kim J, Kalos D, Cutler C, DeFilipp Z, Flowers MED, et al. Ibrutinib for therapy of steroid-refractory chronic graft-versus-host disease: a multicenter real-world analysis. Blood Adv. 2025;9(5):1040-1048. doi: 10.1182/bloodadvances.2024014374

125. Miklos D, Cutler CS, Arora M, Waller EK, Jagasia M, Pusic I, et al. Ibrutinib for chronic graft-versus-host disease after failure of prior therapy. Blood. 2017;130(21):2243-2250. doi: 10.1182/blood-2017-07-793786

126. Moiseev I, Ambron P, Badoglio M, Peczynski C, Basak G, Koenecke C, et al. Steroid-free first line treatment of moderate and severe chronic GVHD: a survey from the Transplant Complications Working Party of the EBMT. Bone Marrow Transplant. 2023; 58(3), 325-327. doi: 10.1038/s41409-022-01881-6

127. Moiseev I, Barabanshikova M, Dotsenko A, Smirnova A, Vlasova Y, Morozova E, Bondarenko S, Kulagin A. First-line steroid-free systemic treatment of acute and chronic graft-versus-host disease after novel prophylaxis regimens. Bone Marrow Transplant. 2023;58(3):257-264. doi: 10.1038/s41409-022-01879-0

128. Pidala J, Onstad L, Martin PJ, Hamilton BK, Cutler C, Kitko CL, et al. Initial therapy for chronic graft-versus-host disease: analysis of practice variation and failure-free survival. Blood Adv. 2021;5:4549-59. doi: 10.1182/bloodadvances.2021005286

129. Pidala J, Hamadani M, Dawson P, Martens M, Alousi AM, Jagasia M, et al. Randomized multicenter trial of sirolimus vs prednisone as initial therapy for standard-risk acute GVHD: the BMT CTN 1501 trial. Blood. 2020;135:97-107. doi: 10.1182/blood.2019003125

130. Solomon SR, Sizemore CA, Ridgeway M, Zhang X, Smith J, Brown S, Holland HK, Morris LE, Bashey A. Corticosteroid-Free Primary Treatment of Chronic Extensive Graft-versus-Host Disease Incorporating Rituximab. Biol Blood Marrow Transplant. 2015;21(9):1576-82. doi: 10.1016/j.bbmt.2015.04.023

131. Moiseev IS, Borzenkova ES, Golubovskaya IK et al. First line single-agent ruxolitinib for grade II-III acute graft-versus-host disease in patients with severe infectious complications: case series. In: The 47th Annual Meeting of the European Society for Blood and Marrow Transplantation: Physicians – Poster Session (P001 – P182). Bone Marrow Transplant. 2021;56(Suppl 1):184-335. doi: 10.1038/s41409