Published in final edited form as:

JAMA Oncol. 2019 May 01; 5(5): 715–722. doi:10.1001/jamaoncol.2018.6278.

Maintenance therapies for Hodgkin and non-Hodgkin lymphomas after autologous transplantation: A consensus project of ASBMT, CIBMTR and LWP-EBMT.

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Financial support: N/A

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Manuscript writing: First draft prepared by Abraham S Kanate and Mehdi Hamadani. All authors helped revised the manuscript.

Final approval of manuscript: All authors

Conflict of interest or Competing interests: None of the authors have any competing interests in the manuscript; except those listed. **P. Dreger** has received honoraria for consultancy for AbbVie, Roche and Janssen; consultancy and speakers' bureau for Gilead; speakers' bureau for Kite Pharma. **M. A. Kharfan-Dabaja** is on the speakers' bureau of Seattle Genetics, Incyte corp, and Alexion Pharmaceuticals**. M. Dreyling** has received honoraria for speakers' bureau, advisory board and trial support for Roche and honorarium from Sandoz. **M. Perales** is a consultant for AbbVie, Incyte, Merck, Novartis and Seattle Genetics. **M. Hamadani** is a consultant for Sanofi Genzyme, Pharmacyclics, ADC Therapeutics, Incyte and MedImmune. Reseach funding: Takeda, Spectrum, Sanofi, Otsuka and Astellas. Speaker's bureau: Sanofi. **S. Smith** is a consultant for Consultant for Roche, AbbVie, Seattle Genetics and Genentech. **A. Herrera** is a consultant for Bristol-Myers Squibb, Genentech, Merck & Co, Pharmacyclics, KiTE Pharma. Resaerch Funding/Grants: Bristol-Myers Squibb, Genentech, Immune Design, Astra Zeneca, Merck & Co, Pharmacyclics, Seattle Genetics, KiTE Pharma. **A. Gopal:** Research Funding: Merck, Teva, BMS, Pfizer, Janssen, SeaGen, Takeda, Spectrum, Gilead, Effector. Paid Consultancy: Janssen, Gilead, Brim Bio, Aptevo, SeagGen, InCyte, Asana. **A. Sureda** has received honoraria for consultancy for Kite Pharma and Sanofi; consultancy and speakers' bureau for Takeda**. M. Shadman** has received honoraria for advisory board from Genetech, AbbVie, Verastem and AstraZeneca. **J. Vose** reports research grant support from Amgen, Acerta Pharma, Astra-Zeneca, Bristol – Myers Squibb, Celgene, Incyte Corp., Kite Pharma, Merck, Novartis, Seattle Genetics, Inc., and consulting/honorarium from Novartis, Abbvie, Epizyme, Roche, Legend Pharmaceuticals, Kyopharm, Sandoz, Vaniam Group, Janssen/Pharmacyclics, Kite Pharma, Acerta and Nordic Nanovector.

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Abstract

Maintenance therapies are often considered as a therapeutic strategy in lymphoma patients following autologous hematopoietic cell transplantation (auto-HCT) to mitigate the risk of disease relapse. With an evolving therapeutic landscape, where novel drugs are moving earlier in therapy lines, evidence relevant to contemporary practice is increasingly limited. The ASBMT, CIBMTR and EBMT jointly convened an expert panel with diverse expertise and geographical representation, to formulate consensus recommendations regarding the use of maintenance/consolidation therapies after auto-HCT in lymphoma patients.

The RAND-modified Delphi method was used to generate consensus statements where ≥75% vote in favor of a recommendation was considered as consensus. The process included three online surveys moderated by an independent methodological expert to ensure anonymity and an in-person meeting. The panel recommended restricting the histological categories covered in this project to Hodgkin lymphoma (HL), mantle cell lymphoma (MCL), diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma. Upon completion of the voting process, the panel generated

22 consensus statements regarding post auto-HCT maintenance/consolidation therapies. The grade A recommendations included endorsement of: (i) brentuximab vedotin (BV) maintenance/consolidation in BV-naïve high-risk HL, (ii) rituximab maintenance in MCL undergoing auto-HCT after first line therapy and (iii) rituximab maintenance in rituximab-naïve FL. (iv) No post auto-HCT maintenance was recommended in DLBCL. The panel also developed consensus statements for important real-world clinical scenarios, where randomized data are lacking to guide clinical practice. In the absence of contemporary evidence-based data, the panel found RAND-modified Delphi methodology effective in providing a rigorous framework for developing consensus recommendations for post auto-HCT maintenance/consolidation therapies in lymphoma.

Keywords

Autologous hematopoietic cell transplantation; maintenance; consolidation; lymphoma; consensus; guidelines

Introduction:

High-dose therapy (HDT) and autologous hematopoietic cell transplantation (auto-HCT) is considered standard treatment for defined indications in classical Hodgkin lymphoma (cHL) and non-Hodgkin lymphoma (NHL)[1,2]. According to the Center for International Blood and Marrow Transplant Registry (CIBMTR) and European Society for Blood and Marrow Transplantation (EBMT) in 2016 ~14,000 lymphoma patients received auto-HCT across North America and Europe[3,4] auto-HCT can provide durable disease control in a subset of patients, disease relapse remains the most common cause of death in lymphoma subjects after undergoing HDT. The majority of relapse events occur within the first 1–3 years following auto-HCT, providing a rationale for post-HCT maintenance/consolidative strategies to mitigate relapse risk[5–8].

In recent years, the lymphoma therapeutic landscape has been in flux with the development of several novel therapies such as monoclonal antibodies (naked, conjugated with drugs, bi-specific T-cell engagers etc.), targeted agents (immunomodulators, proteasome inhibitors, Bruton's tyrosine kinase inhibitors etc.) and immune therapies (checkpoint inhibitors, immune effector cells etc.), that are rapidly finding their way from relapsed/refractory to frontline setting. Considering the time involved in designing and executing clinical trials and procuring regulatory approvals, it is not surprising that studies evaluating post auto-HCT maintenance/consolidation strategies have not been able to keep pace with drug development in lymphomas. This unfortunately means that some trials evaluating post-HCT maintenance strategies in lymphomas enrolled patient populations that are increasingly less relevant to current practice (e.g. rituximab- or brentuximab vedotin-[BV] naïve patients prior to auto-HCT)[5,6]. Moreover, the off-label, off-protocol use of approved anti-lymphoma drugs post auto-HCT as maintenance/consolidation therapies is an increasingly common practice. Clinical practice recommendations or consensus statements addressing the contemporary role of post auto-HCT maintenance/consolidation therapies in lymphomas are not available. Therefore, the American Society of Blood and Marrow Transplantation (ASBMT), CIBMTR and EBMT undertook a joint project to formulate consensus recommendations

regarding the use of post auto-HCT maintenance/consolidation therapies in cHL and NHL. In addition to providing recommendations for post-autologous transplant maintenance/consolidation in lymphoma on scenarios where prospective data are available, the panel also developed consensus statements for a number of important clinical scenarios where randomized data are lacking

Methods:

Panel composition:

The development of practice recommendations was approved by ASBMT, CIBMTR and EBMT, the three leading international organizations in the field of HCT. As an initial step, a steering committee was formed comprising of six members including a project coordinator, representatives of ASBMT, EBMT, CIBMTR and an independent methodologist with expertise in systematic reviews, meta-analysis and the RAND-modified Delphi method. The steering committee was responsible for drafting the protocol, initial draft of consensus statements based on systematic review of the literature and clinical practice considerations and setting up of the expert panel[9]. The aim was to put together a panel with a balanced distribution of 'lymphoma' and 'transplant' experts, in order to have broad expertise and to cover a wide spectrum of views, whilst keeping administrative efforts manageable as previously recommended[10,11]. The panel of experts consisted of physicians with diverse geographical representation and expertise in the field, as demonstrated by their track-record of peer-reviewed publications, leadership of clinical trials relevant to the consensus project and by their involvement in national and international lymphoma or transplant organizations. Additionally, a physician representing a community practice was included in the panel as previously recommended (S. Abutalib)[9]. The final consensus panel consisted of 26 physicians and investigators, including members of the steering committee, except the (non-clinical) independent methodologist, who did not vote on the recommendations (A. Kumar).

Consensus Methodology:

The RAND-modified Delphi method was utilized to generate consensus statements addressing the role of maintenance/consolidation therapies after auto-HCT in lymphoma patients, as recommended by the American Society of Clinical Oncology (ASCO)[9–12]. In the Delphi method, the participants rate the statements anonymously in at least two rounds of evaluations. In the modified version of the method, a face-to-face meeting with presentation of the results precedes the second round of rating[9–11]. Details regarding the systematic step-by-step approach that was involved in this project, are illustrated in Table-1S.

After the panel selection, a *Baseline Demographics and Scope survey* was developed to determine the scope of the project. Participants were invited to submit their suggestions regarding the scope of the consensus project and provide input about the clinical issues relevant to practice (details in Supplemental Appendix). After finalization of the scope of the consensus project, the steering committee conducted a systematic review of the literature to obtain/examine relevant evidence and thereby formulate preliminary consensus statements for first round of voting (details in Supplemental Appendix; Tables 2S; Figures 1S–2S).

The *First Voting Survey* included 22 consensus statements along with supporting evidence (if available). Panel members rated each statement electronically. The steering committee methodologist analyzed and summarized the results, while keeping the individual ratings anonymous. The results of *First Voting Survey*, along with the statements not reaching the threshold of consensus (defined in section below) were presented at the in-person meeting held in conjunction with the 2018 ASBMT and CIBMTR Tandem Meetings at Salt Lake City, UT. Consensus statements that met the predefined criteria for formal consensus were recommended for approval. Statements that failed to achieve predefined criteria for consensus were discussed during the meeting and based on the discussions the statements were modified for re-voting or dropped. The discussion also led to addition of one new statement. The *Second Voting Survey* was sent to all the panel members for rating of the reformulated or newly added statements.

All surveys were administered online using www.Qualtrics.com (Qualtrics LLC, Provo, UT, USA) and results were reviewed and collated independently by the methodological expert. At each step of the process, the electronic survey also allowed the participating members to provide written feedback and comments about each statement. Collated results were shared via email with the consensus panel members in real time after each step was completed to ensure transparency of the process. The final consensus statements were graded based on the strength and level of supporting evidence, according to the Agency of Healthcare Research and Quality (AHRQ) grading[13].

Definitions:

During the voting process, statements forwarded to the consensus panel were rated on a five-point Likert scale (strongly agree=1; somewhat agree=2; neutral=3; somewhat disagree=4 and strongly disagree=5)[9]. A specific statement was defined as having achieved formal consensus, if ≥75% of the panel members voted to strongly agree or agree to the proposed statement.

Results:

Member Participation:

Table-3S describes the baseline characteristics of consensus panel. Included were transplant physicians (>75% of practice time in HCT), non-transplant academic physicians, mixed practitioners and a community-based practitioner. A mixed practice was defined as practitioners devoting approximately 50% of clinical time to HCT and non-transplant related lymphoma, each. In general, panelist participation and response rates were excellent (Figure 3S). At the steering committee level complete participation was noted except for the teleconference where 5 out of 6 members participated. During the voting process, 100% participation was noted for the *Baseline Demographics and Scope*, *First Voting* and *Second Voting* surveys. The in-person meeting was attended by 12 members including 1 member who called in. Two additional members unable to attend in person provided written feedback in advance.

First Voting Survey:

The *First Voting survey* consisted of 22 statements specific to the role of post auto-HCT maintenance/consolidation therapies in following lymphoma histologies; cHL (6 statements), mantle cell lymphoma (MCL, 8 statements), diffuse large B-cell lymphoma (DLBCL, 3 statements) and follicular lymphoma (FL, 5 statements). All but 6 statements (cHL=3, MCL=2 and FL=1) achieved consensus by predefined criteria (Table-5S). In addition to electronically sharing with all panel members, the results of the *First Voting Survey* were also presented at the in-person meeting. The 16 statements meeting the preset definition of consensus were reviewed and approved unanimously. Next, the 6 statements not achieving consensus (<75% agreement) during the prior voting process were reviewed. The ensuing discussion resulted in one statement regarding cHL being abandoned and all other statements being revised. In total 6 statements were proposed (reformulated statements=5, new statement=1; cHL=2, MCL=3, FL=1) for the *Second Voting Survey*. Table-6S shows outcomes of the in-person meeting.

Second Voting Survey:

All statements included in the *Second Voting Survey* (reformulated statements=5, new statement=1), met the predefined criteria for consensus (Table-7S). The final consensus recommendations on post auto-HCT maintenance/consolidation therapies in lymphoma consisting of 22 consensus statements are shown in Table-1 (cHL=5), Table-2 (MCL=9) and Table-3 (DLBCL=3, FL=5).

Discussion:

In clinical scenarios where data from prospective studies are either scarce or unavailable, or in situations where therapeutic advances or new drug indications make patient populations included in published trials less relevant to contemporary clinical practice, formal consensus recommendations can be an invaluable resource in informing clinical decision making. Expert opinions and recommendations in the form of review articles and treatment guidelines, while useful, lack methodological clarity and may be subject to bias. In contrast, formulation of expert recommendations using established approaches, such as the RAND-modified Dephi method, provides a formal, reproducible and systematic process[9,11]. In this project a broadly representative panel of lymphoma and transplant experts with diverse practice experience and geographical representation, endorsed by ASBMT, EBMT and CIBMTR, was formed to provide consensus recommendations on the role of post auto-HCT maintenance/consolidation therapies in lymphomas. It should be noted that the majority of panel members practiced in academic settings (96%) and were transplant physicians with or without non-HCT lymphoma practices, that could be a potential source of confirmation bias. Considering the limitations in existing data and the rapidly expanding repertoire of therapeutic options in lymphoma, such an undertaking was considered a priority and addresses a gap in existing literature. A systematic literature search and expert input identified the gaps in current knowledge and aided the formulation of statements aimed at addressing them. Reported here are 22 practice recommendations addressing the role of post auto-HCT maintenance/consolidation therapies in lymphoma (cHL=5, MCL=9, DLBCL=3, FL=5) (Tables 1–3).

Five consensus statements were generated regarding post auto-HCT maintenance/consolidation therapy in cHL. Taking into account the results of the AETHERA trial[6], the panel recommends *BV maintenance/consolidation after auto-HCT in cHL patients with one or more trial specified risk factors (i.e. primary refractory cHL, relapsed cHL with an initial remission duration of <12months, or extranodal involvement at the start of pre-transplantation salvage chemotherapy) at 1.8mg/Kg intravenously every 3weeks for 16 doses in BV-naïve cHL*. The consensus panel considered the fact that presence of >1 risk factors, per AETHERA trial criteria, might have additive deleterious effects on patient outcomes. For example a CIBMTR report showed that the prognosis of cHL patients with multiple (AETHERA-like) risk factors was extremely poor[14]. Similarly, a post-hoc analysis of the AETHERA study suggested that cHL patients with ≥2 risk factors derived greater progression-free survival (PFS) benefit from BV maintenance after auto-HCT[6]. The facts that routine use of BV maintenance/consolidation has not been shown to improve OS and that it may be associated with higher U.S. healthcare costs compared to surveillance alone, were also considered[15]. However, the panel decided to drop the proposed statement limiting use of BV maintenance/consolidation to patients with >2 risk factors (Table-6S), owing to the lack of high-quality evidence supporting this restriction. Of note, the AETHERA trial only enrolled BV-naïve cHL. With the approval of BV in the frontline setting[16] and increasing use of this agent in pre auto-HCT salvage regimens[17–20] the number of high-risk cHL patients with prior BV exposure is likely going to increase. The panel discussed this important real-world clinical scenario, where high quality prospective data are not available, underscoring the need for consensus recommendations. Accordingly, the panel *recommended the use of BV maintenance/consolidation in patients with prior limited exposure to BV (defined as approximately ≤4–6 cycles)*, undergoing auto-HCT who otherwise meet the AETHERA risk criteria and did not demonstrate prior resistance or intolerance to BV. The panel acknowledge that 'limited prior exposure' in our statement is empiric but agreed to include it as a consideration since no data are available to suggest benefit to BV maintenance/consolidation in patients with prior prolonged exposure to this agent. Pre-autograft PET scan status is an important determinant of patient prognosis[21]. The panel deliberated the possibility of a PET-based risk adapted approach in recommending BV maintenance/consolidation therapy after auto-HCT (Table-6S). Since no robust data are available to show lack of benefit to BV maintenance/consolidation in PET negative high-risk cHL, the panel concluded that *sufficient data do not exist to use the pre-transplant PET (or PET/CT) scan status to guide the use of post auto-HCT BV maintenance/consolidation therapy*.

In MCL patients undergoing upfront auto-HCT after rituximab and cytarabine-containing induction, a randomized trial showed improved PFS and overall survival (OS) with rituximab maintenance compared to observation[7]. This was in line with an earlier retrospective study[22]. Based on these results, the panel achieved consensus to recommend *maintenance rituximab every 2months for a maximum of 3-years (or until unacceptable toxicity or disease relapse/progression [whichever occurs first]) in MCL patients undergoing upfront auto-HCT consolidation following induction with rituximab and cytarabine-based therapy*. The panel wishes to acknowledge that the impact of rituximab maintenance (at least in transplant non-eligible patients), is dependent on the type of frontline therapy, where the

benefit is more pronounced after R-CHOP induction, and may be lacking following fludarabine- or bendamustine-based approaches[23,24]. With this limitation in mind, the panel did reach consensus to *recommend maintenance rituximab in MCL undergoing upfront auto-HCT consolidation, regardless of the induction regimen received* (Grade=C; grading defined in footnote of Table-2), *and in MCL patients undergoing delayed auto-HCT (but without any prior evidence of rituximab resistance* (Grade=C). We acknowledge that only limited retrospective data support these statements[25], and that these statements in large part reflect expert consensus (Grade=C recommendation). No data exist to use the pre-transplant PET or minimal residual disease (MRD) status in determining the need for maintenance rituximab in MCL patients undergoing auto-HCT. Considering the OS benefit conferred by rituximab maintenance in the LYMA trial[7], the panel reached a consensus to *recommend maintenance even in PET or MRD negative patients*. We acknowledge that in MRD negative patients, monitoring and preemptive rituximab therapy in those with molecular relapse has been shown to induce subsequent molecular responses[26]; however, no data exist to show if this preemptive approach is comparable (better, or inferior) to rituximab maintenance. Of note, the recently activated U.S. Intergroup trial () is randomizing MRD negative MCL patients to auto-HCT or no auto-HCT. In this study all MRD negative patients irrespective to study arm, will receive rituximab maintenance for 3-years.

In DLBCL, consensus was achieved to *not recommend rituximab maintenance after auto-HCT in relapsed/refractory DLBCL that was sensitive to rituximab-based salvage approaches*. These recommendations are supported by the final analysis of the CORAL study which showed no event-free survival (EFS) improvement with maintenance rituximab compared to observation[8]. Similarly, the *panel did not endorse maintenance/consolidation therapies in high-risk DLBCL (based on either clinical, histological or genomic criteria)*. While lenalidomide has been shown to improve PFS in elderly DLBCL patients after frontline therapy[27], no data are available to supports its use following auto-HCT. An ongoing randomized, intergroup trial is comparing ibrutinib vs. placebo after auto-HCT in activated B-cell subtype of DLBCL () and may clarify the role of maintenance/consolidation therapy guided by cell-of-origin.

In FL, *the panel endorsed post auto-HCT rituximab maintenance for chemosensitive, relapsed, rituximab-naïve patients*, primarily based on the EBMT study findings (Grade=A)[5]. However, the panel acknowledges that rituximab-naïve status at the time of auto-HCT in FL in the current era would be rare, thus limiting the clinical impact of this statement. While FL patients receiving other CD20 antibodies pre-auto-HCT (e.g. obinutuzumab) but not rituximab, are arguably rituximab-naïve, the panel cautions against extrapolating the above recommendation to this population, especially since the toxicity profile of rituximab maintenance after prior obinutuzumab exposure is not well defined. This scenario is relevant given the survival benefit noted with obinutuzumab in the relapsed (PFS and OS) and frontline (PFS) settings[28,29]. For the clinically more relevant, rituximab-treated FL, no prospective data for the use of maintenance rituximab after auto-HCT exist. Limited retrospective data in this setting suggest improved 3-year PFS (86% vs 46%, p=0.0045) and a trend toward improved OS (96% vs 78%, p=0.059) with maintenance rituximab compared to observation[30]. In addition, a prospective trial as well as an individual patient data meta-analysis showed that rituximab maintenance improved PFS and OS, respectively, in

rituximab-pretreated patients outside the transplant setting[31,32]. However, while the panel recommended *rituximab maintenance in previously rituximab (or other CD20 antibody)-treated FL, (without any prior evidence of rituximab resistance)*, the lack of quality data supporting this consensus statement is also clearly acknowledged (Table-3). Early failure of chemoimmunotherapy (within 2-years) identifies FL patients with a poor prognosis[33]. Recent retrospective data suggest improved outcomes in a subset of such patients with auto-HCT[34–36] but disease relapse remains common. In this challenging subset, rituximab maintenance was recommended with the caveat that patients should not be rituximab refractory.

The panel unanimously voted to *discourage the off-label use of novel agents as post auto-HCT maintenance/consolidation therapies and recommend such use only in the context of a clinical trial*. Throughout the consensus project we adopted a commonly used definition of rituximab-resistance i.e. evidence of relapsed/resistant or progressive disease while on or within 6 months of receiving a rituximab-based regimen[37]. This definition, while routinely used, has the inherent limitation that it cannot distinguish whether the disease is truly resistant to rituximab or to the accompanying chemotherapy agents (in patients getting rituximab + chemotherapy). We also acknowledge that these consensus statements are not a substitute for prospective controlled data, but mainly aim to provide guidance where gaps in knowledge exist. The duration of post-auto-HCT maintenance recommended in the consensus statements is based on available prospective data, however, early cessation of maintenance should be considered for intolerance and toxicities. Disease relapse continues to remain the leading cause of post auto-HCT mortality. With changes in the therapeutic landscape of lymphoma management, incorporation of novel agents in the peri-HCT period to mitigate the risk of therapy failure remains an attractive but under-investigated option.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Final clinical practice guidelines consensus statements on maintenance therapy after high dose therapy and autologous hematopoietic cell transplantation for Hodgkin lymphoma

Consensus Statements - Hodgkin Lymphoma	**Grading of Recommendations**[†]	**Percentage of Panelists in Agreement**
1. The panel recommends post autologous HCT consolidation/maintenance with BV for 16 cycles in BV-naïve classic Hodgkin lymphoma (HL) with at least one or more high-risk features as defined by the AETHERA study.[**]	**A**	**92%**
2. The panel does not recommend post-autologous HCT consolidation/maintenance with BV for HL with prior evidence of disease refractory to BV.	**C**	**96%**
3. The recommended duration of post-auto-HCT BV consolidation/maintenance therapy is for a maximum of 16 cycles every 3 weeks as described in AETHERA trial, or until unacceptable toxicity or disease relapse/progression (whichever occurs first).[**]	**A**	**100%**
4. The panel recommends post autologous HCT consolidation/maintenance with BV in HL with one or more high-risk features as defined by the AETHERA trial and limited prior exposure to BV (~4–6 cycles) preceding the autologous HCT, but without any evidence of BV refractory disease.	**C**	**100%**
5. Sufficient data do not exist to use the pre-autologous-HCT PET (or PET/CT) scan status to guide the use of post autologous HCT consolidation/maintenance therapy with BV for HL with one or more high-risk features as defined by AETHERA Trial.	**C**	**84%**

Abbreviation: HCT – hematopoietic cell transplantation; BV – brentuximab vedontin; PET/CT – positron emission tomography/computed tomography

[**] Consensus statement based on observed PFS benefit, but no OS benefit in randomized trials

[†] **Agency of Healthcare Research and Quality** (AHRQ) grading of recommendations based on level of evidence[13]:

A = There is good research-based evidence to support the recommendation;

B = There is fair research-based evidence to support the recommendation;

C = The recommendation is based on expert opinion and panel consensus:

X = There is evidence of harm from this intervention.

Table 2.

Final clinical practice guidelines consensus statements on maintenance therapy after high dose therapy and autologous hematopoietic cell transplantation for mantle cell lymphoma

Consensus Statements – Mantle Cell Lymphoma	Grading of Recommendations†	Percentage of Panelists in Agreement
1. Regarding upfront autologous HCT for chemosensitive MCL after one line of prior rituximab and cytarabine-containing therapy, the panel recommends maintenance therapy with rituximab every two months for 3 years. *	**A**	**96%**
2. Regarding upfront autologous HCT for chemosensitive MCL, the panel recommends maintenance therapy with rituximab (every two months for 3 years), regardless of the type of pre-transplant induction treatment.	**B**	**92%**
3. Regarding upfront autologous HCT for MCL with a pre-transplantation PET (or PET/CT) scan of Deauville score of 1–3, the panel recommends post-autologous HCT rituximab maintenance therapy.	**C**	**96%**
4. Regarding upfront autologous HCT for chemosensitive MCL with no evidence of pre-transplant minimal residual disease by PCR or next generation sequencing, the panel recommends maintenance therapy with rituximab.	**C**	**77%**
5. Recommended duration of post-auto-HCT rituximab maintenance therapy in MCL is every 2 months for a maximum of three years as described in LYSA trial, or until unacceptable toxicity or disease relapse/progression (whichever occurs first). *	**A**	**92%**
6. After autologous HCT for MCL, maintenance/consolidation therapy with agents other than rituximab (e.g. bortezomib, lenalidomide, BTK inhibitors, BCL2 inhibitors etc.) should only be offered on a clinical trial.	**C**	**100%**
7. The panel does not recommend post autologous HCT rituximab maintenance/consolidation for rituximab-resistant MCL (i.e. relapse or progression of MCL while on, or within 6 months of receiving a rituximab-containing treatment regimen).	**C**	**88%**
8. Regarding MCL patients undergoing a delayed autologous HCT, who have not received rituximab maintenance previously and have demonstrated no evidence of rituximab resistance, the panel recommends post autologous HCT maintenance therapy with rituximab.	**C**	**100%**
9. Regarding MCL patients undergoing a delayed autologous HCT, who have previously received rituximab maintenance, but have demonstrated no evidence of rituximab resistance, the panel recommends post autologous HCT maintenance therapy with rituximab.	**C**	**96%**

Abbreviation: HCT – hematopoietic cell transplantation; PET/CT – positron emission tomography/computed tomography; MCL - mantle cell lymphoma

*Consensus statement based on OS benefit seen in randomized trials

†**Agency of Healthcare Research and Quality** (AHRQ) grading of recommendations based on level of evidence[13]:

A = There is good research-based evidence to support the recommendation;

B = There is fair research-based evidence to support the recommendation;

C = The recommendation is based on expert opinion and panel consensus:

X = There is evidence of harm from this intervention.

Table 3.

Final clinical practice guidelines consensus statements on maintenance therapy after high dose therapy and autologous hematopoietic cell transplantation for diffuse large B-cell and follicular lymphoma

Consensus Statements – Diffuse Large B-cell Lymphoma and Follicular Lymphoma	Grading of Recommendations†	Percentage of Panelists in Agreement
Diffuse Large B-cell Lymphoma		
1. The panel does not recommend post autologous HCT maintenance therapy with rituximab for relapsed/refractory DLBCL that is sensitive to rituximab-based salvage approaches.	**A**	**100%**
2. Regarding autologous HCT for high-risk DLBCL (high-risk IPI score, double/triple hit, double expressor, and/or those with failure of first line therapy within 1 year of diagnosis), either in the upfront or relapsed/refractory setting, the panel does not recommend post autologous HCT maintenance/consolidation therapy with rituximab.	**C**	**100%**
3. Regarding autologous HCT for DLBCL, maintenance/consolidation therapy with novel agents (e.g. monoclonal antibodies other than rituximab, bortezomib, lenalidomide, BTK inhibitors, BCL2 inhibitors, cellular therapies etc.) should only be offered on a clinical trial.	**C**	**100%**
Follicular Lymphoma		
1. The panel recommends post autologous HCT maintenance therapy with rituximab (375 mg/m2 every 2 months for 4 doses) in for chemosensitive, relapsed, rituximab-naïve FL.*	**A**	**81%**
2. The panel recommends post autologous HCT maintenance therapy with rituximab in high-risk FL with early therapy failure (i.e. relapse or progression of disease within 24 months of diagnosis) and no evidence of rituximab resistance.	**C**	**77%**
3. The panel does not recommend post autologous HCT maintenance therapy with rituximab for rituximab-resistant FL (i.e. relapse or progression of FL while on, or within 6 months of receiving a rituximab-based treatment regimen or single agent rituximab)	**C**	**92%**
4. Regarding autologous HCT for FL, maintenance/consolidation therapy with novel agents (e.g. monoclonal antibodies other than rituximab, bortezomib, lenalidomide, PI3K inhibitors, bcl2 inhibitors etc.) should only be offered on a clinical trial.	**C**	**100%**
5. Acknowledging the lack of prospective data, the panel recommends post autologous HCT maintenance therapy with rituximab in chemosensitive, relapsed, previously rituximab (or other CD20 antibody)-treated FL, without any prior evidence of rituximab resistance.	**B**	**84%**

Abbreviation: HCT – hematopoietic cell transplantation; PET/CT – positron emission tomography/computed tomography; DLBCL – diffuse large B-cell lymphoma; IPI – international prognostic index; FL – follicular lymphoma

*Consensus statement based on OS benefit seen in randomized trials

†**Agency of Healthcare Research and Quality** (AHRQ) grading of recommendations based on level of evidence[13]:

A = There is good research-based evidence to support the recommendation;

B = There is fair research-based evidence to support the recommendation;

C = The recommendation is based on expert opinion and panel consensus:

X = There is evidence of harm from this intervention.