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**EANM Focus 4: Consensus on molecular imaging and therapy in  
haematological tumours**

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## **Abstract (250 words)**

### **Introduction**

Given the paucity of high-certainty evidence, and differences in opinion on the use of nuclear medicine for hematological malignancy, we embarked on a consensus process involving key experts in this area. We aimed to assess consensus within a panel of experts on issues related to patient eligibility, imaging techniques, staging and response assessment, follow-up, and treatment decision-making, and to provide interim guidance by our expert consensus.

### **Methods**

We used three-stage consensus process. First, we systematically reviewed and appraised the quality of existing evidence. Second, based on the literature review we generated a list of 153 statements to be agreed/disagreed with. Third, the 153 statements were scored by a panel of 26 experts on a 1 (strongly disagree) to 9 (strongly agree) Likert scale in a two-round e-Delphi. The RAND/UCLA appropriateness method was used for analysis.

### **Results**

Between one and 14 systematic reviews were identified on each topic. All were rated as low-moderate quality. After two rounds of voting, there was consensus on 90% of the statements.

### **Discussion and conclusions**

There was consensus on most statements. More studies are required to define the optimal sequence for treatment assessment of MM using [<sup>18</sup>F]FDG PET and the nuclear medicine community is not ready yet to introduce volumetric parameters (MTV and TLG) and AI and ML and radiomics into the routine practice because the evidence is not strong enough. Our expert opinion-based consensus guidance can be used in the interim whilst the community awaits the accumulation of better certainty in the evidence base.

**Key words:** haematological tumours; myeloma; lymphoma; molecular imaging; radionuclide therapy



## **Introduction**

The use of nuclear medicine techniques has changed the standard of care in many clinical situations. Hematological malignancies represent one of the first entities in which nuclear medicine has had a major impact by advancing fundamental changes in both diagnostic and therapeutic practices within the last 2-3 decades <sup>1</sup>.

To consolidate what constitutes best clinical practice, and to harmonize the guidance on currently uncertain topics, the European Association of Nuclear Medicine (EANM) initiated the Focus 4 meeting dedicated to hematological malignancies.. The Focus meetings are an annual event organized by the EANM to provide guidance on nuclear medicine topics where evidence is weak or lacking, with three previous successful iterations tackling molecular imaging and theranostics in prostate cancer <sup>2</sup>, dementia<sup>3</sup>, and neuroendocrine tumours <sup>4</sup>.

Within Focus 4, all medical disciplines responsible for hematological malignancy patient care were brought together to interpret the current evidence and to provide practical guidance.

Given that there may be differences of opinion on how to interpret the current evidence in hematological malignancies and apply it in clinical practice, our aim in this project was to assess consensus robustly and transparently within a panel of experts on issues related to patient eligibility, imaging techniques, staging, treatment decision-making, response assessment, and follow-up, and to provide interim guidance by our expert consensus.

## **Methods**

### **Overview**

To meet the project's aims, a three-stage consensus process was used. First, relevant medical/scientific literature was systematically searched for, and the quality of the evidence summarized (see supplementary file 1). Second, based on this literature review, the Focus 4 co-chairs (CN and CK) and Focus 4 Scientific Committee members (KH and JK) drafted a list of positively framed statements, which could be agreed or disagreed with and could not be currently answered by the available evidence. Finally, in a two-round modified online

Delphi (e-Delphi) process, the expert panel was invited to score the statements, indicating agreement, disagreement, uncertainty, or ‘unable to score’ (see below). A face-to-face consensus conference was planned to take place after the second e-Delphi round, to ratify the results, discuss statements for which consensus remained lacking, and to rescore those statements. However, due to the COVID-19 pandemic, that meeting, originally planned for February 2021, was postponed for 1 year, and then, in January 2022, cancelled. A further pragmatic consideration in cancelling the in-person meeting was that consensus thresholds had been met for 90% of the statements after the two online rounds. Hence, an additional scoring round appeared to be of limited value.

The participants in the e-Delphi process comprised experts in all aspects of the management of haematological tumours, including, but not limited to, molecular imaging and radionuclide therapy. Experts were identified via authorship of published research on haematological tumours. Thirty experts were invited to participate, 28 initially completed round one, but two experts withdrew and asked for their data to be deleted, and the remaining 26 completed both rounds. Their self-identified areas of expertise can be seen in table 1.

**Table 1: Expert panel and self-identified field of expertise**

<b>Name</b>	<b>Field of expertise</b>
Ronald Boellaard	Nuclear Imaging Physics
Live Eikenes	Medical Physics
Stefano Luminari	Hematology
Martin Hutchings	Hematology-Oncology
Bruce Cheson	Hematology-Oncology
Wojciech Jurczak	Hematology
Christian Baues	Radiation Oncology
Carsten Kobe	Nuclear Medicine
Irène Buvat	Medical Physics
Ulrich Dührsen	Hematology-Oncology
Andreas Buck	Nuclear Medicine
Françoise Kraeber-Bodéré	Nuclear medicine and PET

Egesta Lopci	Nuclear Medicine
Cristina Nanni	Nuclear Medicine and PET
Pier Luigi Zinzani	Hematology
Robert Chrzan	Radiology
Nadia Withofs	Nuclear Medicine
Bettina Baeßler	Radiology
Anne-Ségolène Cottreau	Nuclear Medicine
Björn Chapuy	Hematology and Lymphoma Genomics
Elena Zamagni	Hematology
George Mikhaeel	Oncology
Marcel Nijland	Hematology
Peter Borchmann	Oncology
Paula Rodriguez Otero	Hematology
Josée M. Zijlstra	hematology

### **Systematic literature review**

The PubMed database was searched through December 11<sup>th</sup>, 2021 for English-language literature published from 01/01/2010 regarding molecular imaging and therapy of haematological malignancies. Within these topics, separate searches were made regarding areas that were envisioned to be covered by statements developed by the Scientific Committee for the panelists to score. Terms employed in the search and a summary of the results appear in Supplementary file 1. To increase the search's sensitivity, PubMed filters were omitted.

In the first instance, systematic reviews, meta-analyses, evidence-based guidelines, and evidence-based review articles related to the respective potential statement topics were included. If no systematic reviews were found, a search of primary studies published since 01/01/2010 was performed. When possible, European Society for Medical Oncology (ESMO) clinical practice guidelines on haematological malignancies were retrieved and their bibliographies were checked against the search results to ensure that influential studies were not missed.

The quality of the retrieved systematic reviews was assessed using AMSTAR 2 criteria <sup>5</sup> (results shown in Supplementary file 1). Four weeks before scoring the statements the papers retrieved in the literature search were made available to the expert panelists alongside tables summarizing the quality assessment of the systematic reviews.

### **Modified Delphi process**

In round one of the modified e-Delphi, participants were emailed a link to an online survey containing 153 statements organized in five thematic tracks with sub-themes (the statements and the organization within tracks can be seen in Table 2). Each statement was phrased so that panelists could indicate their strength of agreement with it on a 9-point Likert scale ranging from 1 (strongly disagree) to 9 (strongly agree), and the middle point '5' was labelled 'neither agree nor disagree'. Panelists were urged only to choose a score in the 4–6 if they felt that they had sufficient information and expertise to opine on the statement and truly neither agreed nor disagreed; otherwise, they were asked to choose a separate category not included in the Likert scale, 'unable to score'. Participants were permitted to comment on any statement in round 1 and to submit statements for consideration by the scientific committee that they believed should be added for round 2 scoring. Three such statements were suggested, one of which was added (see Table 2, statement added in track 1 but numbered 999 in analysis to maintain sequencing across rounds for all other statements).

In round two of the modified e-Delphi, participants were reminded of their own round one score and shown the distribution of other panelists' scores for each statement. They were asked to re-score the 153 original items and to score the additional statement. DelphiManager software, developed and maintained by the Core Outcome Measures for Effectiveness Trials (COMET) Initiative, was used to undertake the e-Delphi survey

(COMET. DelphiManager. [cited 14 April 2022] Available from: <http://www.comet-initiative.org/delphimanager/>. Accessed 14 April 2022).

### **e-Delphi data analysis**

The e-Delphi data were analysed following the RAND/UCLA appropriateness method, which has been shown to provide robust results regardless of panel size.<sup>6</sup> For each statement, the panel's median score and 30<sup>th</sup>–70<sup>th</sup> interpercentile range (IPR) were calculated. The IPR adjusted for symmetry (IPRAS) was calculated, using the formula (IPRAS = 2.35 + [asymmetry index \* 1.5]). In that formula, the asymmetry index is defined as the absolute difference between the central point of the IPR and 5 (5 being the central point on the 1–9 scoring scale). If IPR < IPRAS, this is interpreted as no extreme dispersion of scores, i.e., the median score is considered to represent “consensus”. Median scores in the range 1–3 were categorized as ‘disagree’, 4–6 as ‘uncertain’, and 7–9 as ‘agree’. Analysis was done using Stata 11 (StataCorp LP, College Station, TX, USA).

## **Results/Findings**

### **Systematic literature review**

The complete results of the systematic literature review are reported in supplementary file 1. Briefly, each track focused on a different thematic topic, and had sub-themes within, hence the inclusion/exclusion criteria were necessarily different for each topic. Between 1 and 14 systematic reviews were included for each sub-theme. The included systematic reviews were rated as moderate to low quality on AMSTAR2 assessment, with none meeting the criteria for ‘high’ quality.

## **Modified Delphi**

There was ‘consensus’ (agree, disagree or uncertain) on 133/153 (87%), and ‘no consensus’ on 20/153 (13%) statements after round 1. There was ‘consensus’ on 139/154 (90%) and ‘no consensus’ on 15/154 (10%) of statements after round two. The full results can be viewed in table 2.

The median [range] of participants choosing ‘unable to score’ was 6 [1-13] and although in some statements, 1 or 2 additional participants scored more the item in the second round (see table 2) the median and range were the same in round 2.

The results of the e-Delphi after the second round are shown in table 2, including the median, interpercentile range, direction of agreement, and consensus status. We do not describe the results further here and instead focus on summarizing them and their implication in the discussion.

## **Discussion**

### **Non-Hodgkin Lymphoma (NHL) (statements 1-28)**

#### **Staging and Response assessment using [<sup>18</sup>F]FDG PET/CT**

There was strong agreement that all the following subgroups should undergo staging with [<sup>18</sup>F]FDG PET/CT in routine clinical practice: all patients with diffuse large B-cell lymphoma (DLBCL) and possibly other [<sup>18</sup>F]FDG-avid aggressive NHL; all patients with follicular lymphoma (grade I-IIIa) and possibly other [<sup>18</sup>F]FDG-avid indolent NHL including

those with early stage; and patients with indolent lymphoma with clinical suspicion of high-grade transformation and questionable early stage. The panel also agreed that: [<sup>18</sup>F]FDG PET/CT should be performed and can guide biopsy in indolent lymphoma if there is a suspicion of transformation, and that staging DLBCL or other [<sup>18</sup>F]FDG-avid aggressive NHL with [<sup>18</sup>F]FDG PET/CT can be used to show bone marrow involvement and replace bone marrow biopsy in most cases.

In consideration of response assessment in NHL, the panel agreed that in patients with DLBCL and possibly other [<sup>18</sup>F]FDG avid aggressive NHL [<sup>18</sup>F]FDG PET/CT should be performed for response assessment at interim staging; but there was no consensus regarding interim staging in patients with follicular lymphoma (grade I-IIIa) and possibly other [<sup>18</sup>F]FDG avid indolent NHL. After chemotherapy, the panel strongly agreed that [<sup>18</sup>F]FDG PET/CT should be performed in both patients with DLBCL and possibly other [<sup>18</sup>F]FDG-avid aggressive NHL, and in patients with follicular lymphoma (grade I-IIIa) and possibly other [<sup>18</sup>F]FDG-avid indolent NHL.

Considering that [<sup>18</sup>F]FDG PET/CT includes low-dose CT for attenuation correction, no consensus was reached to recommend contrast enhanced Computed Tomography [ceCT] for response assessment in patients with DLBCL or other [<sup>18</sup>F]FDG-avid aggressive NHL, but, concerning the statement suggested by a participant in round one, and scored by all in round two, the panel agreed that the size of lymphoma residual masses should be reported even if there is no [<sup>18</sup>F]FDG uptake.

On the topic of [<sup>18</sup>F]FDG PET/CT in decision-making for radiotherapy, there was agreement that the end-of-chemotherapy [<sup>18</sup>F]FDG PET/CT provides information necessary to decide for or against radiotherapy in DLBCL and possibly other [<sup>18</sup>F]FDG-avid aggressive NHL; but

in patients with follicular lymphoma (grade I-IIIa) and possibly other [<sup>18</sup>F]FDG-avid indolent NHL the panel was uncertain whether to base the decision for or against radiotherapy on [<sup>18</sup>F]FDG PET/CT.

### **Follow up**

There was agreement within the panel that during follow-up of aggressive NHL, clinical examination should be performed, however, the panel disagreed that [<sup>18</sup>F]FDG PET/CT, ceCT and/or MRI should be performed routinely for up to 24 months.

In the follow-up of indolent NHL, clinical examination should be performed; the panel voted against the routine use of ceCT, MRI, or [<sup>18</sup>F]FDG PET/CT for up to 24 months. In contrast, ceCT and/or MRI and [<sup>18</sup>F]FDG PET/CT should be performed in case of suspected relapse, [<sup>18</sup>F]FDG PET/CT in case of [<sup>18</sup>F]FDG avid NHL.

### **Potential for innovation**

Despite the fact IPS is the most robust clinical risk factor, there was no consensus within the panel regarding whether Ann Arbor and IPI classification should be further improved or not, even though PET assessed MTV supplemented IPI (IMPI) has recently been described and outperformed the IPI<sup>7</sup>. However, the panel strongly agreed the current staging system may be improved by new PET features, such as dissemination features and metabolic tumour volume (MTVI). Furthermore, they agreed that non-imaging blood-based markers are worth further investigation to better guide treatment decisions in lymphoma.

### **Hodgkin Lymphoma (HL) (statements 29-56)**



### **Staging and Response Assessment using [<sup>18</sup>F]FDG PET/CT**

The panel strongly agreed that all patients should undergo staging using [<sup>18</sup>F]FDG PET/CT before start of treatment, without any restriction, and that [<sup>18</sup>F]FDG PET/CT should be used in HL patients to exclude bone marrow involvement instead of bone marrow biopsy.

Furthermore, the panel strongly agreed that [<sup>18</sup>F]FDG PET/CT is necessary for response assessment at interim staging in advanced stage HL, after 2 cycles of chemotherapy and that the use of [<sup>18</sup>F]FDG PET/CT in HL should be tailored depending on the therapy protocol. For all HL patients, not only in advanced stages, [<sup>18</sup>F]FDG PET/CT is seen as the central guiding tool to decide whether or not to perform radiotherapy.

### **Follow-up**

Agreement was achieved that follow-up should be restricted to clinical examination and laboratory blood testing in the routine setting, while ceCT, MRI, ultrasound, and/or [<sup>18</sup>F]FDG PET/CT should not be performed routinely. In contrast, in cases of suspected relapse [<sup>18</sup>F]FDG PET/CT and ceCT should be performed in addition to clinical examination and routine laboratory testing, while routine ultrasound does not appear mandatory for all patients.

### **Potential for innovation**

The panel strongly agreed that Ann Arbor classification does not reflect current diagnostic opportunities and that the Ann Arbor classification alone is inadequate for staging. However, there was no consensus within the panel regarding whether Ann Arbor and IPI classification should be further improved or not.

The aim for standardized imaging was not sufficient for consensus recommendation for EARL-accreditation of all PET/CT scanners, but it was acknowledged that the combination

of non-imaging blood-based biomarkers and [<sup>18</sup>F]FDG PET/CT in HL is promising to further improve response prediction.

Standardization in lymphoma imaging, staging and response assessment may have improved since the Lugano classification<sup>8</sup> and International Conference on Malignant Lymphoma Working Group recommendations<sup>9</sup>. The current consensus lends weight to these recommendations.

### **Myeloma (statements 57 – 123)**

Many of the ‘no consensus’ statements, 7/1 (46%), pertained to the MM section. The one with most controversy was the sequence of PET/CT in active MM. Regarding the staging of suspected active multiple myeloma (MM), panelists agreed on the use of [<sup>18</sup>F]FDG PET/CT in all patients (with both secretory and non-secretory disease) regardless of the result of other imaging procedures such as Low Dose CT (LDCT) and MRI. On the contrary, the panel’s opinion on Smouldering Myeloma or MGUS was that no [<sup>18</sup>F]FDG PET/CT should be performed, except for those patients with one small lesion/equivocal findings at LDCT or MRI. No definitive agreement was reached on the timepoints of [<sup>18</sup>F]FDG PET/CT scan during active disease history.

Strong agreement was found on the need for a standardized report at staging, outlining: the number and size of lytic lesions on LDCT; fractures on LDCT; the exact number of [<sup>18</sup>F]FDG PET/CT positive focal lesions grouped (0, 1-3, >), the SUV<sub>max</sub> of the hottest focal lesion, increased diffuse uptake in the bone marrow, and locations with significantly increased risk of fracture on LDCT. It was also agreed that a standard report was required during and after therapy to document: the number and size of lytic lesions on LDCT independent of [<sup>18</sup>F]FDG uptake only if increased as compared to baseline; fractures on LDCT; the exact number of

[<sup>18</sup>F]FDG PET/CT positive focal lesions grouped (0, 1-3, >3) and compared to baseline, the SUV<sub>max</sub> of the hottest focal lesion, increased diffuse uptake in the bone marrow, decrease in number and size of [<sup>18</sup>F]FDG PET/CT positive focal lesions (bony, paramedullary, extramedullary) along with the Deauville Score of the hottest focal lesion, the change of SUV<sub>max</sub> and/or DS (Deauville Score) of the hottest focal lesion and decrease of diffuse uptake in the bone marrow.

The panel agreed that all the patients with solitary plasmacytoma (SP) located in the bone or in extramedullary areas should undergo an [<sup>18</sup>F]FDG PET/CT, including those with only one lesion detected by whole-body MRI. However, there was no consensus among the panelists on the opportunity to include an [<sup>18</sup>F]FDG PET/CT in the patient's work-up depending on its availability but they agreed that the use of [<sup>18</sup>F]FDG PET/CT should not be dependent on approval/label.

The panel agreed that there is currently not enough evidence supporting the need to perform any other tracer but [<sup>18</sup>F]FDG [98-102] in routine clinical practice due to current lack of data.

On the topic of [<sup>18</sup>F]FDG PET/CT field of view, the panel agreed that this should cover from top of the head to feet, arms down. Regarding the reporting system at staging, the panel agreed that diffuse bone marrow uptake should be reported when it is visually higher than the normal liver uptake but the utility of increased diffuse uptake in the bone marrow of limbs associated to that of the axial skeleton remains uncertain.

The measurement of TMTV and total lesion glycolysis (TLG) was considered to be confined to clinical trials so far and should not be routinely reported. At the end of therapy, a complete normalisation of [<sup>18</sup>F]FDG PET/CT in Multiple Myeloma can be seen if the uptake in

previous hot focal lesions and bone marrow are not measurable or are visually below the liver and no new lytic lesions in LDCT images are present.

For the evaluation of minimal residual disease, [ $^{18}\text{F}$ ]FDG PET/CT should be performed even in patients with negative multiparametric flow cytometry or genomic tests on bone marrow aspiration. There was no consensus on whether [ $^{18}\text{F}$ ]FDG PET/CT is fundamental if multiparametric flow cytometry genomic tests are positive on bone marrow aspiration. [ $^{18}\text{F}$ ]FDG PET/CT and multiparametric flow cytometry bone marrow genomic tests provide a stronger patient stratification as compared to each single technique taken alone.

### **Nuclear medicine and therapy in haematological malignancies**

Whilst considering the role of nuclear medical therapies it was agreed that therapy with [ $^{90}\text{Y}$ ]Y-ibritumomab tiuxetan ibritumomab tiuxetan (ZEVALIN<sup>®</sup>) has not become a standard for the majority of NHL patients but can be used as an option for patients experiencing relapsed or refractory follicular lymphoma. In contrast, the role of [ $^{68}\text{Ga}$ ]Ga-CXCR4-ligand remained somewhat unclear even in such multiple myeloma patients in which CXCR4-expression might be clinically relevant in the light of a subsequent radiotheranostic approach. Here it appears that the [ $^{68}\text{Ga}$ ]Ga-CXCR-4 specific radioligand treatment for multiple myeloma has not yet become an international standard yet and more clinical data is needed.

So far, the relatively new tracers [ $^{68}\text{Ga}$ ]Ga-FAPI and [ $^{18}\text{F}$ ]F-fluciclovine are not seen as potential candidates for staging lymphoma patients, even if they may support a specific theranostic treatment.

The panel agreed that new treatment opportunities, such as immune checkpoint inhibition,

might have an influence on [<sup>18</sup>F]FDG PET/CT imaging and they were interested concerning the clinical introduction of a [<sup>68</sup>Ga]Ga-PD-1 specific PET radiotracer. However, in the meantime [<sup>18</sup>F]FDG PET/CT remains the standard for staging before treatments start and under ongoing treatment, e.g. after 4 and 8 months.

### **Radiomics, artificial intelligence (AI) incl. machine learning (ML), and standardization**

Presently, the panel did not identify a radiomic signature that should be included in standard PET reporting. The panel agreed that the use of radiomics requires standardization of PET images or of PET features, including MTV and TLG measurement to provide robust implementation of the diagnostic work-up. Interestingly, there was no consensus on the point of whether staging HL and NHL using [<sup>18</sup>F]FDG PET/CT should only be done in centers with EARL-accredited PET/CT scanners, which would ensure the comparability and harmonization of image quality.

Although AI including ML are promising techniques to assist image analysis, their use is not yet recommended to guide therapeutic decisions. The panel acknowledged prognostic information obtained by AI and ML is not always fully explainable, limiting its translation to clinical routine.

### **Limitations**

Expert consensus is low-certainty evidence, but we have controlled for group processes and dominant voices through anonymized voting and controlled feedback in the e-Delphi process. Furthermore, for some statements a relatively large proportion of the participants chose ‘unable to score’. This can be explained by the wide-ranging scope of the consensus statements and that no one panelist was likely to be an expert in every topic. Even though

personal face to face communication between panelists was restricted, the wide variety of experts in the field nominated by the European Society of Nuclear Medicine provides a high breadth and depth of expertise and communication was encouraged via email in during the process of discussing results and preparing the manuscript . We feel that on balance the wide scope of the consensus statements and their implications for improving interim guidance is warranted despite some panelists not feeling well enough informed to answer some questions.

In short, there was consensus within the expert panel on 90% of the statements. The take home messages are that more studies are required to define the optimal sequence for treatment assessment of MM using FDG PET and that the nuclear medicine community is preparing to introduce volumetric parameters (MTV and TLG) and AI and ML and radiomics into the routine practice.

## **Conclusion**

In short, there was consensus within the expert panel on 90% of the statements. The take home messages are that more studies are required to define the optimal sequence for treatment assessment of MM using FDG PET and that the nuclear medicine community is preparing to introduce volumetric parameters (MTV and TLG) and AI and ML and radiomics into the routine practice.

When introducing new methods for diagnostics and therapy in hematological malignancies we expect high-certainty evidence in order to further improve diagnostic accuracy and patients' treatment. We have witnessed how and to which extent [<sup>18</sup>F]FDG PET/CT has become a standard in hematological malignancies, having a major influence in many clinical situations. Nevertheless, there is still room for improvement concerning cure rates, side effects and long-term sequelae of the treatment, as well as patient's health related quality of life and satisfaction with their care. Although there is potential for new targets, new tracers and new analyses of imaging and biomarkers, none are currently fit for purpose. Our expert

opinion-based consensus guidance can be used in the interim whilst the community awaits the accumulation of better certainty in the evidence base.

### **Contributors**

KH and JK co-chaired the EANM Focus 4 Project and contributed equally to this work. CN and CK served on the Focus 4 Scientific Committee and contributed equally to this work. All the authors were members of the EANM Focus 4 expert panel, completed both rounds of the e-Delphi process, and participated in the drafting and critical review of the paper, and approved the paper's submission.

### **Declaration of interests**

CN, CK, BB, CB, RB, Bche, RC, A-SC, LE, FK-B, WJ, SL, NGM, NW, and JMZ declare no conflicts. IB has received research grants from Dosisoft, GE Healthcare, and Siemens Healthineers, and is a member of the Society of Nuclear Medicine and Molecular Imaging Artificial Intelligence Task Force. BC has received research support from GWT, Technical University of Dresden, and won a 2021 Gilead Oncology Award to support his research. BC also has received honoraria for serving as an advisory board member for ADC, Bristol Myers Squibb, Regeneron, Incyte and Roche, and for lectures from AstraZeneca, Bristol Myers Squibb, and Roche. BC received a travel grant from Gilead, has applied for a patent for a method of molecular subclassification of diffuse large B-cell lymphoma, and has volunteered as Speaker of the Aggressive Lymphoma Working Group and as a Steering Board member of the German Lymphoma Alliance. UD has received institutional funding from Celgene and has served as a Data Safety Monitoring Board member for Amgen and Avencell Europe. EL has received grants from AIRC and the Italian Ministry of Health, royalties from Springer, and honoraria for lectures at the European Society of Molecular Imaging and Therapy and Molecular Imaging & Therapy Congresses. MN has received a research grant from Takeda.

PR-O has received honoraria from Amgen, Bristol-Myers Squibb, Glaxo SmithKline, Janssen, Regeneron, and Sanofi, and served as a Data Safety Monitoring Board member for Bristol-Myers Squibb, Glaxo SmithKline, Janssen, Oncopeptides, Pfizer, Sanofi, and Takeda. EZ has received honoraria from Amgen, Celgene/Bristol-Myers Squibb, Janssen, and Takeda. PLZ has received honoraria from AstraZeneca, Beigene, Bristol-Myers Squibb, Eusapharma, Gilead, Incyte, Janssen, Kyowa Kirin, Merck, Mundipharma, Novartis, Roche, Sanofi, Takeda and has participated on Advisory Boards or Data Safety Monitoring Boards for these firms. KH reports personal fees from Adacap, Ktis Oncology, Amgen, Bayer, Curium, Endocyte, Ipsen, GE Healthcare, Novartis, Pharma15, Siemens Healthineers, SIRTEX, Theragnostics, and ymabs, personal fees and other from Sofie Biosciences, grants and personal fees from BTG, and non-financial support from ABX, outside the submitted work. JK has received consulting fees from Telix and has served as a Data Safety Monitoring Board member for Novartis. EZ has received honoraria from Amgen, Celgene/Bristol-Myers Squibb, Janssen, and Takeda.

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