

National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Mogamulizumab for treated mycosis fungoides or Sézary syndrome cutaneous T-cell lymphoma ID1405

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Wording	Kyowa Kirin	<p>We believe the remit as written; “To appraise the clinical and cost effectiveness of mogamulizumab within its marketing authorisation for treated mycosis fungoides (MF) or Sézary syndrome (SS) T-cell lymphoma.”; is appropriate. However, for clarity, we recommend that “cutaneous” should be inserted before “T-cell lymphoma”, here and elsewhere in the draft scope.</p> <p>In addition, to align more closely with the marketing authorisation, we recommend replacing “treated” with “previously treated with at least one prior systemic therapy”.</p>	<p>The term cutaneous have been added to the remit and in other parts of the draft scope.</p> <p>The population section in the draft scope states “Adults with mycosis fungoides or Sézary syndrome cutaneous T-cell lymphoma following at least one prior systemic therapy.”</p>
	British Association of Dermatologists	Yes	Comment noted.

Section	Consultee/ Commentator	Comments [sic]	Action
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	Draft remit/appraisal objective To appraise the clinical and cost effectiveness of mogamulizumab within its marketing authorisation for previously treated cutaneous T-cell lymphoma.	The term cutaneous has been added to the remit and in other parts of the draft scope.
	Takeda	No Comment	N/A
Timing Issues	Kyowa Kirin	Not applicable	Comment noted.
	British Association of Dermatologists	There are limited options for patients with cutaneous T cell lymphoma with a large unmet clinical need.	Comment noted.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	There is an unmet need for effective treatments for CTCL.	Comment noted.
	Takeda	No Comment	N/A
	Kyowa Kirin	None	N/A

Section	Consultee/ Commentator	Comments [sic]	Action
Additional comments on the draft remit	British Association of Dermatologists	No	Comment noted
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	No comments received	N/A
	Takeda	No comments received	N/A

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Kyowa Kirin	<p>The current description of the treatment pathway does not include mention of brentuximab vedotin which, following NICE Technology Appraisal (TA) 577, is now recommended for treating CD30-positive CTCL, after at least one prior systemic therapy if patients have MF stage \geqIIB, primary cutaneous anaplastic large cell lymphoma or SS.</p> <p>We would also recommend review of this as part of the treatment pathway: "Stem cell or bone marrow transplant (such as allogeneic stem cell transplant) may also be a treatment option for some people (for example those with advanced disease, a poor response to systemic therapy, multiple relapses or a short remission)."</p>	Brentuximab vedotin has now been added to the background section of the scope.

Section	Consultee/ Commentator	Comments [sic]	Action
		This aligns with TA577 Final Appraisal Determination (FAD) 3.2 wording: “the clinical experts noted that allogeneic stem cell transplants may consolidate treatment response to achieve durable remission, or possibly cure, and should be considered for certain patients with advanced CTCL”	
	British Association of Dermatologists	It is perhaps worth emphasising that it is an incurable disease and current therapeutic options have significant toxicities limiting ability to achieve long term disease control	Comment noted. The background section of the scope is intended to be a brief overview of the condition and treatment options. No changes required.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	<p>There are no curative treatments for MF/SS. Current treatments have response rates around 40% and response duration is typically short < 1 year. Patients tend to be treated with multiple consecutive therapies and treatment options are frequently exhausted [ref Trautinger 2017]</p> <p>There are extremely limited treatment options in MF/SS and these are almost never curative as such there is a shortage of treatment options.</p> <p>Patients with MF/SS have a high symptom burden with painful, itchy skin lesions which are disfiguring. At best, current treatments provide partial responses and complete responses are rare.</p>	Comment noted. The background section of the scope is intended to be a brief overview of the condition and treatment options. No changes required.
	Takeda	<p>Please include brentuximab vedotin as an available and NICE recommended therapy for the treatment of CD30-positive CTCL.</p> <p>Suggested wording:</p>	Brentuximab vedotin is now included in the background and

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		<p>Brentuximab vedotin received a marketing authorisation from the EMA in December 2017 for the treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) who require systemic therapy. It had been available in the UK via a compassionate use program and has received a positive recommendation from NICE for routine commissioning in April 2019.</p> <p>On 24th April 2019, NICE issued a positive Technology Appraisal Guidance [TA577] recommending brentuximab vedotin as an option for treating CD30 positive cutaneous T cell lymphoma (CTCL) after at least 1 systemic therapy in adults. The positive recommendation is for mycosis fungoides stage IIB or over, primary cutaneous anaplastic large cell lymphoma (pcALCL) or Sézary syndrome.</p> <p>Brentuximab vedotin is an antibody-drug conjugate (ADC), a targeted therapy, that delivers an antineoplastic agent (MMAE) that results in apoptotic cell death selectively in CD30-expressing tumour cells. Binding of the ADC to CD30 on the cell surface initiates internalisation of the ADC-CD30 complex, which then traffics to the lysosomal compartment. Within the cell, MMAE is released via proteolytic cleavage. Binding of MMAE to tubulin disrupts the microtubule network within the cell, induces cell cycle arrest and results in apoptotic death of the CD30-expressing tumour cell.</p>	comparator section of the scope.
The technology/ intervention	Kyowa Kirin	<p>For clarity, we suggest the Page 2 text: “is indicated for the treatment of adult patients with treated mycosis fungoides or Sézary syndrome T-cell lymphoma.” be replaced with the following: “is indicated for the treatment of adult patients with mycosis fungoides or Sézary syndrome who have received at least one prior systemic therapy.”</p>	Comment noted. The draft scope has been changed to reflect this.

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	British Association of Dermatologists	Yes	Comment noted.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	Moga is a CCR4 monoclonal antibody which is effective treatment for MF and SS	The technology section describes the mechanism of action of the treatment. The committee will consider all clinical evidence related to the technology.
	Takeda	No Comment	N/A
Population	Kyowa Kirin	<p>The pivotal study for mogamulizumab in previously treated CTCL, the MAJORIC study¹, included patients with Stage IB+ mycosis fungoides (MF) or Sézary syndrome (SS), and stratified randomisation by disease type (MF versus SS) and disease stage (IB-II vs III-IV). Of the included population across both treated arms, there were 20-30% stage IB-IIA MF and the remaining were stage IIB+ disease or SS</p> <p>In TA577, “advanced disease” cutaneous T-cell lymphoma (CTCL) patients were defined as those with mycosis fungoides Stage IIB+ disease, primary cutaneous anaplastic large cell lymphoma and Sézary syndrome).</p>	Comments noted. No change to the scope required.

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		<p>We share the TA577 committee’s understanding that compared with earlier stages of CTCL, advanced disease is associated with poorer prognosis, lower survival and lower quality of life (FAD 3.2).</p> <p>We believe that the evidence for mogamulizumab is compelling within and across its licensed remit, reflecting the group that MAVORIC was powered to test the effectiveness of mogamulizumab within, and that this population has been defined appropriately in the draft scope. However, we believe it appropriate to present results from prespecified MAVORIC subgroups and agree with the definition and description of advanced disease in TA577.</p>	
	British Association of Dermatologists	Yes	Comment noted.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	<p>Yes</p> <p>Are there any subgroups of people in whom mogamulizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?</p> <p>The MAVORIC trial is the largest randomised controlled trial to date in CTCL, and in particular included patients with SS who were not included in the other large randomised trial ALCANZA, and so this group should perhaps be considered in a separate subgroup.</p>	Comments noted.
	Takeda	No Comment	N/A
Comparators	Kyowa Kirin	We agree with the tabular description of comparators as “Established management without mogamulizumab”.	Comments noted. No action required.

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		<p>We share the TA577 committee's February 2019 understanding that retinoid (bexarotene), interferon alpha or single-agent chemotherapy (methotrexate) are the systemic agents first offered to CTCL patients previously treated with a systemic therapy (FAD 3.4), with treatment selection based on various factors including history of and response to, previous systemic treatments.</p> <p>We are systematically collecting evidence on the validity of the comparator arm of MAVORIC (vorinostat 400mg once daily) as proxy clinical effectiveness evidence for established management without mogamulizumab. It is worth noting that the differential response rate on mogamulizumab versus vorinostat does provide evidence of a treatment effect for mogamulizumab.</p> <p>Following TA577, brentuximab vedotin is routinely available to CD30-positive CTCL adult patients after at least one systemic therapy, if they have stage IIB+ disease and subject to a commercial access agreement.</p> <p>The Alcanza2 trial of brentuximab vedotin has recruited adult patients with CD30-positive MF or primary cutaneous anaplastic large-cell lymphoma (pcALCL) who had been previously treated with systemic therapy or radiotherapy. Approximately 70% of the trial cohort was stage IA-IIB MF and ~25% was pcALCL with no SS patients. The MAVORIC trial on the other hand recruited ~45% SS with no stage IA MF and no pcALCL patients. The stark differences in mechanism of action, patient populations as well as their pre-treatment profiles and study end points coupled with additional important differences in the timings for response and progression assessments make meaningful clinical effectiveness comparisons between the two treatments (brentuximab vedotin and mogamulizumab) prohibitively difficult</p>	
	British Association of Dermatologists	Yes	Comment noted.

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	Leukaemia Care	Whilst we appreciate there is no standard of care, clarity on which comparators are most appropriate is needed. Clarity of where this treatment is positioned in relation to other treatments and whether this treatment aims to treat symptoms or systemic disease is needed.	Comments noted. These issues will be addressed during the course of the appraisal.
	The Royal College of Pathologists and British Society for Haematology	<p>This would be triple therapy (bexarotene plus interferon alpha plus photopheresis)</p> <p>This has been kept vague in the scope “established clinical management without mogamulizumab” which I think is ok due to the variation in approaches used nationally and internationally (Quaglino Ann Oncol 2017 28(10) 2517-2525). Comparators would be as per the different treatment options as listed in the British Guidelines (British Journal of Dermatology 2019 180: 496-526) plus brentuximab given the recent NICE approval following the publication of the ALCANZA trial.</p> <p>Which treatments are considered to be established clinical practice in the NHS for treated mycosis fungoides or Sézary syndrome T-cell lymphoma? How should established clinical management be defined?</p> <p>As above, I would adopt the British Guidelines as the established clinical practice in the NHS. There is a paucity of randomised controlled trials in MF/SS and no clear systemic therapy that leads to a survival benefit to suggest a suitable sequence of treatments making it difficult to be dogmatic about established clinical management.</p>	Comments noted. No changes required.
	Takeda	We note the following proposed comparators: Established clinical management without mogamulizumab.	Comments noted. Brentuximab vedotin is included in the current wording within the

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		<p>Takeda would like to request that brentuximab vedotin be added and considered as a comparator to the single technology appraisal of Mogamulizumab for treated mycosis fungoides or Sézary syndrome T-cell lymphoma ID1405.</p> <p>NICE issued a positive Technology Appraisal Guidance [TA577] recommending brentuximab vedotin as an option for treating CD30 positive cutaneous T cell lymphoma (CTCL) after at least 1 systemic therapy in adults. The positive recommendation is for mycosis fungoides stage IIB or over, primary cutaneous anaplastic large cell lymphoma (pcALCL) or Sézary syndrome. This guidance was issued on April 24th 2019, however brentuximab vedotin has been available through a compassionate use program since December 2016, and would now be considered as a part of standard care in the UK.</p> <p>The guidelines for the management of CTCL published by the UK Cutaneous Lymphoma Group (UKCLG) and British Association of Dermatologists (BAD) in 2018 recommend brentuximab vedotin as a second line treatment for mycosis fungoides, pcALCL and Sezary syndrome. The guidelines can be accessed via the following link: http://www.bad.org.uk/shared/get-file.ashx?id=6265&itemtype=document</p> <p>Based on the draft population within this scope [ID1405], mycosis fungoides and Sézary syndrome, there is an overlap in the main populations under consideration and therefore brentuximab vedotin is a relevant comparator.</p>	<p>scope as “established clinical management without mogamulizumab”. No change required.</p>
Outcomes	Kyowa Kirin	<p>We believe so, though also note time to next therapy (TTNT) be included as a meaningful outcome measure for this appraisal.</p> <p>MAVORIC demonstrated mogamulizumab was superior to vorinostat in progression-free survival (median 7.7 vs 3.1 months, $P < 0.0001$)¹, and post-hoc analysis of intention-to-treat data highlighted further patient- and health system-relevant benefit in extending time to any next therapy excluding</p>	<p>Comments noted. The listed outcomes in the draft scope are not intended to be exhaustive. Time to next treatment has now</p>

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		topical steroids or focal radiation by a greater extent (median 11.0 versus 3.5 months, P<0.0001) ³	been included in the draft scope.
	British Association of Dermatologists	Yes	Comment noted.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	<p>Yes and skindex 29 which is very relevant for MF/SS patients as well as pruritus score</p> <p>Are the outcomes listed appropriate? Yes but note that the study was not powered for overall survival and allowed cross-over of patients from the comparator arm to mogamulizumab thus focus should not be placed on OS rather the other measures. The other point to consider is not only the duration of response which will have an impact on the burden of disease/ symptoms but also the speed of response which will also have an impact.</p> <p>Where do you consider mogamulizumab will fit into the existing NICE pathway, non-Hodgkin's lymphoma? As a treatment option in cutaneous T cell lymphoma</p>	<p>Comment noted.</p> <p>Comments noted. No change required.</p>
	Takeda	All outcome measures have been captured.	Comments noted.
Economic analysis	Kyowa Kirin	The time horizon that is sufficiently long to reflect any differences in costs or outcomes between the technologies being compared in this appraisal is a lifetime horizon.	Comments noted. The appraisal committee will take into account the

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		The most challenging aspect of the reference case for robust and fair economic appraisal of mogamulizumab in CTCL is the use of EuroQol 5-dimension (EQ-5D) questionnaires as the preferred measurement tool for health-related quality of life. In MAVORIC, patients completed both EQ-5D-3L and Skindex-29 questionnaires, but as recognised by the TA577 committee, neither tool fully captures all skin-related and physiological symptoms of CTCL (FAD 3.13).	measures used to capture health-related quality of life and assess issues related to this.
	British Association of Dermatologists	No comments received	N/A
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	patients with MF/SS suffer from poor quality of life and prolonged periods where skin disease affects function including ability to work. There is a huge unmet need for more and better treatments.	Comments noted.
	Takeda	No comment.	N/A
Equality and Diversity	Kyowa Kirin	We do not think that the proposed remit and scope need to change to meet these aims.	Comment noted.
	British Association of Dermatologists	No comments received	N/A
	Leukaemia Care	No comments received	N/A

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	The Royal College of Pathologists and British Society for Haematology	no	Comment noted.
	Takeda	No comment.	N/A
Other considerations	Kyowa Kirin	Carer burden is also under review for this appraisal.	Comment noted. The committee will decide on the relevant perspective for the appraisal.
	British Association of Dermatologists	No comments received	N/A
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	Moga provides an effective treatment option for MF/SS with improvement in skin, blood and nodal compartments as well as improved QOL. The progression free survival has also been shown to be superior to vorinostat. Moga provides a treatment option for even the most heavily pre-treated patients with responses not related to number / type of previous therapies	Comments noted. The committee will appraise the technology based on the evidence base.
	Takeda	In the Related NICE recommendations and NICE Pathways section of the draft scope the NICE technology appraisal of brentuximab vedotin for treating CD30-positive cutaneous T-cell lymphoma [ID1190] is listed as "in development", however this appraisal has concluded.	Comments noted. Brentuximab vedotin has now been added to this section.

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		<p>This final guidance for this appraisal is as follows:</p> <p>Brentuximab vedotin is recommended as an option for treating CD30 positive cutaneous T cell lymphoma (CTCL) after at least 1 systemic therapy in adults, only if:</p> <ul style="list-style-type: none"> • they have mycosis fungoides stage IIB or over, primary cutaneous anaplastic large cell lymphoma or Sézary syndrome and • the company provides brentuximab vedotin according to the commercial arrangement. <p>The final NICE guidance was published on April 24th 2019 as Technology Appraisal Guidance TA557 https://www.nice.org.uk/guidance/ta577</p>	
Innovation	Kyowa Kirin	<p>The introduction of mogamulizumab, as an immunotherapy will represent a step-change in managing MF and SS for which approved treatment options are limited and duration of response is often short. None of the treatments available to date targets CCR4 (CC chemokine receptor 4) and therefore mogamulizumab is an innovative treatment option, through its unique mechanism of action. It targets all disease compartments (skin, blood, lymph nodes and viscera) and provides a durable response to patients who require systemic therapy and have failed to sufficiently respond to available systemic treatments including those approved in the UK.</p> <p>The safety data from MAVORIC demonstrates that mogamulizumab is a well-tolerated treatment, which is also an important consideration given the toxicities associated with existing treatment options approved and used routinely in the EU.</p> <p>This step change in care is expected to affect both patients and the health system by relieving patient symptoms and improving patient and carer quality</p>	<p>Comments noted. The appraisal committee will consider whether mogamulizumab is innovative.</p> <p>The appraisal committee will take into account the measures used to capture health-related quality of life and assess issues related to this.</p>

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		<p>of life while reducing the time and resource burden of care on the NHS. It is inevitable, given (i) the limitations of available health-related quality of life tools to capture the range of symptoms that affect CTCL patients and their carers and (ii) the limited data availability generally in this small, high-need patient group, that significant and substantial health-related benefits that are likely to be unaccounted for in the QALY calculation.</p> <p>We do also want to highlight the challenges of the lack of availability of a sensitive enough tool to ascertain quality of life in this rare haematological malignancy indication. This was commented on in TA577, section 3.13: “The clinical experts explained that neither tool fully captures all skin related and physiological symptoms of CTCL. They further explained that a health-related quality-of-life tool specific to CTCL was being developed but was not yet available.”</p> <p>Given the limitations of data in this area, the Appraisal Committee will be reliant to an extent upon the accounts of patient, carer and clinician experts to capture expected benefits.</p>	
	British Association of Dermatologists	Yes, there is a large unmet clinical need.	Comment noted. The appraisal committee will consider whether mogamulizumab is innovative.
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and	Do you consider mogamulizumab to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might	Comment noted. The appraisal committee will consider whether

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		<p>Abstract from ASH 2018 Blood 2018 132:3592- this abstract focused on the impact of the symptoms/ PROMs for patients enrolled onto this trial.</p> <p>Kim Y, Bagot M, Pinter-Brown L, et al. Mogamulizumab versus Vorinostat in Previously Treated Cutaneous T-Cell Lymphoma. Lancet Oncol. 2018 Sep;19(9):1192-1204</p> <p>Efficacy of mogamulizumab by prior systemic therapy in patients with previously treated cutaneous T-cell lymphoma in the phase 3 MAVORIC study</p> <p>Authors: Steven Horwitz, MD1; Alison J. Moskowitz, MD1; Pierluigi Porcu, MD3; Pier Luigi Zinzani, MD, PhD4 TBD</p> <p>ABSTRACT</p> <p>Aims: Mycosis fungoides (MF)/ Sezary syndrome (SS) patients receive multiple lines of therapy of varying classes during their disease course. The phase 3 MAVORIC study (NCT01728805) demonstrated that mogamulizumab (Moga), a monoclonal antibody against CCR4, was superior to vorinostat in progression free survival (PFS) and overall response rate (ORR) in previously treated patients with MF/SS. Preclinical studies have suggested CCR4 levels may be downregulated by histone deacetylase inhibitors (HDACi) thus this post hoc analysis of MAVORIC examined the effect of prior systemic therapies (PST), specifically prior HDACi, on clinical response to Moga.</p> <p>Methods: 372 MF/SS patients who had failed ≥1 systemic therapy were randomized to Moga 1.0 mg/kg i.v. or Vor 400 mg orally until disease</p>	

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		<p>progression or unacceptable tolerability. PFS and ORR were assessed by prior HDACi exposure and other prior-therapy subgroups using Cox proportional hazards and logistic regression models, respectively.</p> <p>Results: MAVORIC enrolled 186 patients in each arm, with an average age of 63 years; baseline characteristics including number and types of PST were balanced. Forty nine (26.3%) Moga randomized patients had prior exposure to any HDACi; 34 (18.3%) Vor randomized patients had prior HDACi. The most common immediate PST in the Moga arm were oral bexarotene (n=104; 56%), interferon (n=54; 29%), methotrexate (n=46; 25%) and romidepsin (n=28; 15%). In HDACi-exposed patients, median PFS was 5.40 (95% CI, 2.8, 10.4) and 2.13 (95% CI, 1.3, 3.9) months for Moga and Vor, respectively; confirmed ORR was 22.4% and 0%, respectively. In HDACi-naïve patients, median PFS was 9.37 (95% CI, 6.7, 14.0) and 3.33 (95% CI, 2.9, 4.7) months in Moga and Vor, respectively; confirmed ORR was 29.9% and 5.9%, respectively. PST subgroup analyses based on immune activity demonstrated no effect, either by type or time from treatment, on Moga responses.</p> <p>Conclusions: These post hoc analyses suggest that clinical responses to Moga in MAVORIC did not appear to be affected by prior systemic therapies, including any prior HDACi exposure.</p> <p>Efficacy of mogamulizumab in previously treated patients with less advanced mycosis fungoides: results from the MAVORIC study</p> <p>Authors (≤35 author limit): Julia Scarisbrick, MD1, Larisa J. Geskin, MD2, Martine Bagot, MD3, David C. Fisher, MD4, Craig Elmets, MD5, Madeleine</p>	

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		<p>Duvic, MD6, Marie Beylot-Barry, MD7, Ellen J. Kim, MD8, Junji Moriya, MS9, Mollie Leoni, MD9, Pier Luigi Zinzani, MD10</p> <p>Introduction: In the MAVORIC Phase 3 study, patients (pts) with previously treated mycosis fungoides (MF)/Sezary syndrome (SS) stage IB-IVB who received mogamulizumab (MOGA; Poteligeo®) had significantly prolonged progression-free survival (7.7 vs 3.1 months; $p < 0.0001$) and greater overall response rates (ORR) compared to pts on vorinostat (VORI) (Kim YH, et al. Lancet Oncol 2018). Less advanced MF (stage IB/IIA) is a chronic skin malignancy that can involve blood and nodes and may require many lines of systemic therapy over the disease course with a reduced quality of life. This post-hoc analysis specifically examined efficacy and safety of the recently approved MOGA in stage IB/IIA MF pts.</p> <p>Methods: In MAVORIC, stage IB-IVB MF/SS pts (n=372) who were treated with ≥ 1 prior systemic therapy were randomized to MOGA or oral VORI. In the post-hoc analysis, time to next treatment (TTNT) was defined as time to any therapy excluding topical steroids or focal radiation treatment. ORR was based on global composite response in 4 disease compartments – skin, blood, lymph nodes, and viscera – achieved at 2 consecutive visits at least 8 weeks apart. Individual compartment responses were also assessed.</p> <p>Results: A total of 85 pts with stage IB/IIA MF were included (MOGA, IB n=15, IIA n=21; VORI, IB n=27, IIA n=22). Overall, 79% (33/42) of IB pts and 84% (36/43) of IIA pts had received ≥ 2 prior systemic therapies, and 24% (10/42) of IB pts and 28% (12/43) of IIA pts had received ≥ 6 prior systemic therapies. Median TTNT with MOGA in IB pts was 11.5 months (mo) (95% CI, 1.4, 16.0) compared to 3.1 mo (95% CI, 2.7, 5.3) with VORI; in IIA pts, median TTNT was 10.1 mo (95% CI, 5.5, 12.6) and 4.9 mo (95% CI, 2.4, 8.0),</p>	

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		<p>respectively. ORR in IB pts receiving MOGA and VORI was 20% (3/15) and 18.5% (5/27), respectively; ORR in IIA was 19% (4/21) and 0% (0/22), respectively. With respect to stage IB and IIA, compartmental response rates with MOGA were: skin (20% [3/15], 38% [8/21]), blood (0% [0/2], 75% [6/8]), and lymph node (0% [0/0], 15% [3/20]), respectively. Adverse events were generally manageable and consistent with the ITT population.</p> <p>Conclusions: This post-hoc analysis of TTNT, ORR, and compartmental response in stage IB/IIA demonstrates meaningful clinical benefit with MOGA in early stage MF pts previously treated with systemic therapies despite MAVORIC not being powered to determine treatment effect by disease stage.</p>	
	Takeda	No comment.	Comment noted.
Questions for consultation	Kyowa Kirin	We believe each of the questions for consultation have been covered in the above sections.	Comment noted.
	British Association of Dermatologists	No comments received.	N/A
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	Moga should be considered alongside other immunotherapies for second line systemic therapy in MF/SS ahead of chemotherapy which has a low durable response in MF/SS and may lead to increased susceptibility to infection.	Comments noted. Not changes to the scope required.

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	Takeda	Most of the comments have been addressed above. Please note Takeda's comments on the comparator, related NICE guidance and background information.	Comments noted. please see related responses.
Additional comments on the draft scope	Kyowa Kirin	None to add	Comment noted.
	British Association of Dermatologists	No comments received.	N/A
	Leukaemia Care	No comments received	N/A
	The Royal College of Pathologists and British Society for Haematology	No comments received	N/A
	Takeda	No comments received	N/A

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

Lymphoma Action