Mogamulizumab in Patients with Mycosis Fungoides or Sézary Syndrome: Update on the German Non-Interventional MINT Study

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Background

- Mogamulizumab (moga) is a defucosylated, humanised monoclonal antibody targeting CC chemokine receptor (CCR4)
- CCR4 is skin-homing and an overexpressed biomarker in cutaneous T-cell lymphoma (CTCL)[1]
- Moga depletes tumour cells in CTCL via enhanced antibody-dependent cellular cytotoxicity, owing to moga's defucosylation
- Mycosis fungoides (MF) and Sézary syndrome (SS) are the most studied subtypes of CTCL, a heterogeneous group of rare extranodal T-cell lymphomas[2]
- Moga was first approved by the EMA in 2018 based on MAVORIC, a large, multicentre (N=372), randomized, phase 3 trial, and is indicated in Europe for the treatment of adult patients (pts) with MF or SS who have received at least one prior systemic therapy[3]
- Moga is approved for use in ≥50 countries globally

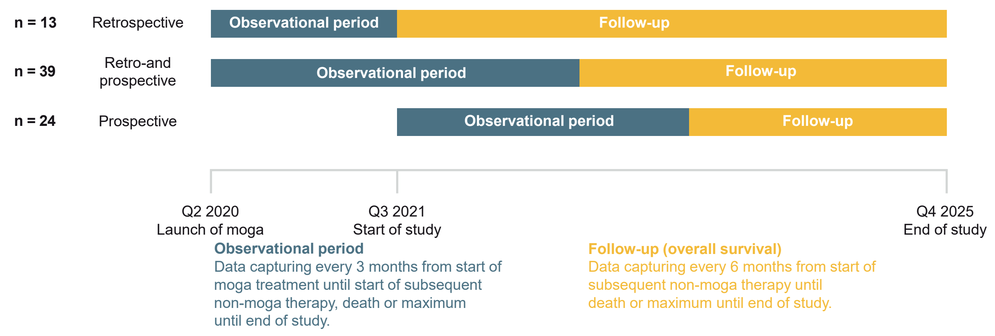
Study Objectives

- MINT is a real-world, combined retrospective and prospective, multicentre, non-interventional study to assess the effectiveness and tolerability of moga in German clinical practice
  - Here, we present the second interim analyses conducted for pts with ≥3 months, observational data (n=76)

Methods

- Data were collected from medical records of participating pts at 17 study centres
- Pts were required to have been selected for moga treatment in routine practice according to the approved indications prior to inclusion
- The patient observational and follow-up periods were as described in **Figure 1**

Figure 1. Study design. For this interim analysis, the data cut-off was 2 May 2024.



Moga, mogamulizumab; pts, patients.

Primary Endpoint

- Time to next treatment (TTNT; defined as start of moga to start of new therapy [not including topical steroids/focal radiation] after moga discontinuation)

Secondary Endpoints

- Progression-free survival (PFS)
- Best overall response rate (bORR): Global complete or partial response as assessed by investigators
- Duration of overall response (DOR)
- Compartmental response rates (lymph nodes, skin, peripheral blood, and viscera)
- Time to additional treatments
- Blood tumour burden
- Health-related quality of life (HRQoL) measured by Skindex-29 and ItchyQoL at 3, 6, 9, and 12 months
- Diagnostic discrepancy rate
- MF subtype proportion
- Dose modification/interruption
- Adverse events (AEs)

Safety

- Treatment-emergent adverse events (TEAEs) were recorded from the start of moga treatment to 30 days after the last dose

Results

Patient Demographics and Baseline Characteristics (Table 1)

- Median follow-up time (min, max) was 20.5 (1.0, 56.3) months
- The distribution of pts with MF and SS was equal, with each group comprising 50% (n=38)
  - In pts with MF, blood tumour burden at the start of moga treatment was B0: 16 (21.1) and B1: 14 (18.4)

Table. Baseline patient characteristics

	N = 76
Mean age, years (SD)	67.4 (12.4)
Sex, n (%)	
Female	33 (43.4)
Male	43 (56.6)
Initial diagnosis, n (%)	
SS	38 (50.0)
MF	38 (50.0)
MF subtype, n (%)	
Classical	28 (36.8)
Folliculotropic	5 (6.6)
Pagetoid reticulosis	1 (1.3)
Other	4 (5.3)
Disease stage at moga start, n (%)	
IB	9 (11.8)
IIA	1 (1.3)
IIB	13 (17.1)
IIIA	2 (2.6)
IIIB	8 (10.5)
IVA (NOS)	3 (3.9)
IVA1	23 (30.3)
IVA2	12 (15.8)
IVB	4 (5.3)
Missing	1 (1.3)
Blood tumour burden at moga start, n (%)	
B0	16 (21.1)
B1	14 (18.4)
B2	17 (22.4)
Missing	29 (38.2)

MF, mycosis fungoides; NOS, not otherwise specified; SD, standard deviation; SS, Sézary syndrome.

Concomitant Treatments (Table 2)

- Antineoplastic concomitant treatments were received by 32.9% (n=25) pts
- Most commonly (>5%) extracorporeal photopheresis (17.1%), total skin electron beam (TSEB); (including low-dose TSEB; 7.9%) and radiotherapy (not TSEB; 6.6%)

Table 2. Concomitant treatments

	N = 76
Concomitant[a] MF/SS treatment received, n (%)	
Antihistamines	20 (26.3)
Topical corticosteroids	17 (22.4)
Systemic corticosteroids	8 (10.5)
TSEB (inc. low-dose TSEB)	6 (7.9)
Radiotherapy (not TSEB)	5 (6.6)
ECP	13 (17.1)
Bexarotene	2 (2.6)
Etoposide	2 (2.6)
(PEG) IFN alfa-2a	1 (1.3)
UV-B/nbUV-B	1 (1.3)
Chlormethine	1 (1.3)
PUVA	1 (1.3)

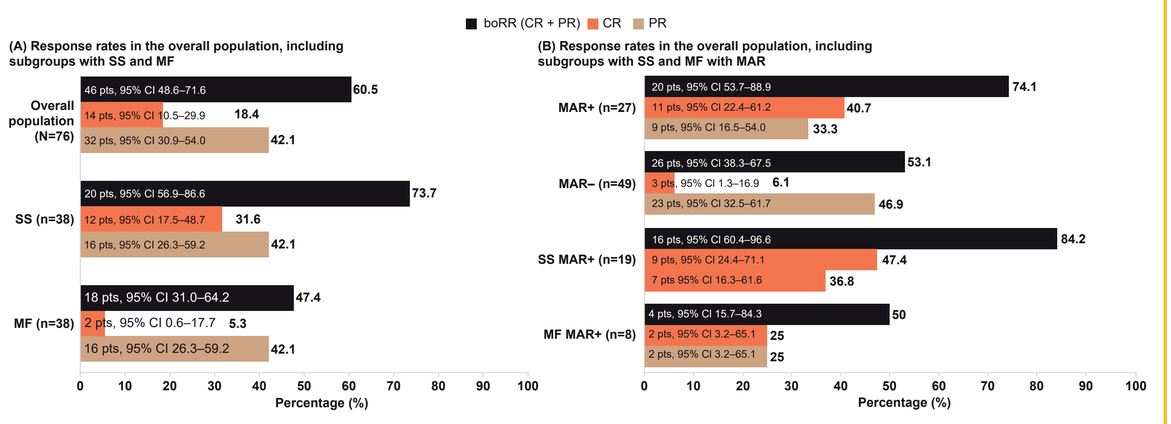
ECP, extracorporeal photopheresis; IFN, interferon; MF, mycosis fungoides; nbUV-B, narrowband ultraviolet B; PEG, pegylated; SD, standard deviation; SS, Sézary syndrome; TSEB, total skin electron beam; PUVA, psoralen + ultraviolet A; UV-B, ultraviolet B.
[a]Defined as therapies started for indication of 'MF/SS' prior to moga start and continued thereafter, or with a start date on/after mogamulizumab start. Multiple concomitant treatments possible.

Patient Outcomes

- Median overall TTNT (95% confidence interval [CI]) was 20.2 (11.0–34.8) months
- Median duration of moga treatment in all pts was 6.27 months[a], it was 6.60 months in pts with mogamulizumab-associated rash (MAR) and 5.77 months in pts without MAR
- bORR was 60.5% (46/76): 73.7% (28/38) for SS and 47.4% (18/38) for MF (**Figure 2A**)
- MAR occurred in 27 pts: 19 (50.0%) SS and 8 (21.1%) MF pts, and bORR was higher for pts with MAR (74.1%, 95% CI 53.7–88.9) vs pts without MAR (53.1%, 95% CI 38.3–67.5) (**Figure 2B**)
  - bORR in pts with SS, and MAR was 84.2% (16/19) and 50% (4/8) in those with MF and MAR

[a]The total population of pts represents all three cohorts: retrospective (4.60 months), retro- and prospective (10.30 months), and prospective (4.60 months).

Figure 2. Patient outcomes



bORR, best overall response rate; CI, confidence interval; CR, complete remission, MAR, moga-associated rash; MF, Mycosis fungoides; PR, partial response; pts, patients; SS, Sézary syndrome.

Treatment-Related TEAEs (Table 3)

- Lymphopenia or 'lymphocyte count decreased' and drug eruption or rash were the most commonly reported Grade ≥3 treatment-related TEAEs and serious Grade ≥3 treatment-related TEAEs
- The most common TEAE leading to discontinuation was drug eruption or rash (15.8% [12/76])
  - Infusion reaction were rare (1.3% [1/76])

Table 3. Treatment-related TEAEs

Preferred Terms	N = 76
Grade ≥3, n (%)	26 (34.2)
Lymphopenia or 'lymphocyte count decreased'	12 (15.8)
Drug eruption or rash	10 (13.2)
Serious Grade ≥3, n (%)	11 (14.5)
Lymphopenia or 'lymphocyte count decreased'	2 (2.6)
Drug eruption or rash	3 (3.9)
TEAEs of special interest	
Infections and infestations	1 (1.3)
Infusion-related reactions	2 (2.6)
Tumour-lysis syndrome	1 (1.3)

TEAEs, treatment-emergent adverse events.

Conclusions

- Clinical responses were seen in pts with MF and SS; with ≥30% receiving concomitant further systemic or skin-directed antineoplastic therapies
- No new safety signals were observed; however, due to the inherent limitations of RWE studies, these results should be interpreted with caution
  - Drug eruption was the most common cause of discontinuation in the phase 3 MAVORIC trial
  - Lymphopenia is an expected pharmacological effect of moga
- Real world evidence shows that combination therapies are frequently used
  - Further investigation is warranted to better understand which combinations represent most benefits for pts

References

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Conflicts of interest

LO, SH, ED and **AB** do not have anything to declare. **CA** has been a consultant for 4SC, Helsinn Healthcare, Kyowa Kirin, Recordati, and Takeda Pharmaceuticals; **NB** has been a consultant for Kyowa Kirin, received honoraria from Kyowa Kirin and Recordati and travel expenses from Kyowa Kirin, Recordati, and Takea Pharmaceuticals; **GD** has been a consultant for Helsinn Healthcare, Kyowa Kirin, Mallinckrodat Pharmaceuticals, Recordati, and Takeda Pharmaceuticals; **MS** has been a consultant for Bristol Myers Squibb, Immunocore, Kyowa Kirin, Merck Sharp & Dohme, Novartis, Pierre Fabre, Recordati, and Sun Pharma; **MO** has received honoraria from Kyowa Kirin; **K-CK** has been a consultant for Kyowa Kirin, Recordati and Vetter Pharma, received honoraria/other support from Bristol-Myers Squibb, Kyowa Kirin, Novartis, Pierre Fabre and Sun Pharma, and is a member of the board of directors/advisory committees for Novartis; **JN** has been a consultant for Actelion, Biogen, Innate Pharma, Kyowa Kirin, Mallinckrodt Pharmaceuticals, Novartis, Recordati, Takeda Pharmaceuticals, TEVA and UCB Pharma and received research funding from Kyowa Kirin; **MW** has been a consultant for Kyowa Kirin, Recordati, Stemline Therapeutics and Takeda Pharmaceuticals; JH has received speaker honoraria from Bristol Myers Squibb, Delcath, Immunocore, Merck Sharp & Dohme, Novartis, Pierre Fabre, Sanofi, Sunpharma and has received honoraria for participation in strategic advisory boards for Pierre Fabre and Sunpharma and travel grants for Bristol-Myers Squibb, Lovance amd Sunpharma; **CM** has received honoraria from AstraZeneca, Bristol-Myers Squibb, Merck Sharp & Dohme, Pierre Fabra, Recrodati, and research funding from German Research Foundation and Society of MSK and had other professional associations with Kyowa Kirin, Novartis, Sun Pharma; PT has been a consultant for Almirall, Bristol-Myers Squibb, Biofrontera, Kyowa Kirin, L'Oréal, Merck Sharp & Dohme, Novartis, Pierre Fabre, Sanofi and 4SC and other professional associations with Bristol Myers Squibb; **C-DK** has been a consultant for Actelion, Innate Pharma, Kyowa Kirin Recordati and Takeda Pharmaceuticals, and received honoraria from Kyowa Kirin, Recordati, Sanofi, Stemline, Takeda Pharmaceuticals and participated in clinical trails with 4SC AG, IQVia, Kyowa Kirin, Novartis, Sciderm, Takeda Pharmaceuticals; CW has been a consultant for Amgen, AstraZeneca, Bristol Meyers Squibb, Curevac, Merck Sharp & Dohme; Novaartis, Pierre Fabre, Roche Pharma, Sanofi and Therakos.. **FH** has received honoraria from Pierre Fabre, Kyowa Kirin and Sanofi; **MCM**: Permanent employee of Kyowa Kirin International, PLC. **AD**: Permanent employee of Kyowa Kirin GmbH

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