Restarting Subcutaneous MabThera after Treatment Interruption

This letter responds to your request for information on MabThera SC® (rituximab and hyaluronidase human) and restarting MabThera subcutaneous administration after a treatment interruption.

Mabthera SC treatment interruptions allowed in Roche pivotal trials

Roche has no recommendations on when to restart MabThera SC after a treatment interruption. We cannot provide therapeutic recommendations for individual patients.

However, treatment interruptions were allowed in pivotal studies to allow patients to recover from hematological toxicities, infections, or other clinical conditions that precluded treatment according to institutional practice.

Table 1 provides a summary of the pivotal trial study designs.

Indication	1L FL	1L CLL	1L DLBCL
Study Name	SABRINA[1,2]	SAWYER[3,4]	MABEASE[5]
Study design	MabThera SC vs. IV (combined with CHOP or CVP)	MabThera SC vs. IV (combined with FC)	MabThera SC vs. IV (combined with CHOP)
Study objective	Investigator-accessed ORR at completion of combo treatment w/ chemotherapy	Non-inferiority of PK profile of MabThera SC vs. IV	Investigator-accessed CR/CRu at completion of combo treatment w/ chemotherapy
Subcutaneous administration schedule	Every 8 weeks	Every 28 days	Every 21 days
Duration of allowed delay	Up to 8 weeks	Up to 4 weeks	Not specified
Condition under which delay was allowed	Any clinical condition that precluded treatment according to institutional practice	For all 3 Mabthera treatment arms when recovering from hematological toxicities or infections	N/A
Maximum delay between 2 MabThera doses	16 weeks	8 weeks	Not specified

Abbreviations: CHOP=chemotherapy regimen consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone; CLL=chronic lymphocytic leukemia; CR=complete response; CRu=unconfirmed complete response; CVP=chemotherapy regimen consisting of cyclophosphamide, vincristine sulfate, and prednisone; DLBCL=diffuse large b-cell lymphoma; FC=chemo regimen consisting of fludarabine and cyclophosphamide; FL=follicular lymphoma; IV=intravenous; N/A=not available; ORR=objective response rate (CR,CRu, & PR); PR=Partial Response; PK=Pharmacokinetics, SC=subcutaneous; 1L=1st line/previously untreated

Safety considerations for restarting MabThera SC

Clinicians should consider individual patient factors such as previous IRRs or ARRs, tumor burden and peripheral B-cell counts when deciding how to restart Mabthera SC after a dose interruption.

Previous infusion-related reactions (IRRs) and administration-related reactions (ARRs)

Patients are at the highest risk of experiencing an IRR from MabThera IV at Cycle 1. Patients with a high tumor burden may be at higher risk of developing severe IRRs.[6]

Restarting MabThera treatment with an IV-first dose after an extended delay or interruption of MabThera SC may help to manage ARRs because of the ability to control slowing or stopping the IV infusion.[6]

The rate of IRRs after varying intervals of treatment interruptions were not evaluated in pivotal studies.[6]

References

1. Davies A, Merli F, Mihaljević B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomised, open-label, phase 3 trial. Lancet Haematol 2017;4:e272-e282. https://www.ncbi.nlm.nih.gov/pubmed/28476440

2. Roche Internal Clinical Study Report. (Accessed on 29 Jun 2023).

3. Assouline S, Buccheri V, Delmer A, et al. Pharmacokinetics, safety, and efficacy of subcutaneous versus intravenous rituximab plus chemotherapy as treatment for chronic lymphocytic leukaemia (SAWYER): a phase 1b, open-label, randomised controlled non-inferiority trial. Lancet Haematol 2016;3:e128-38. https://www.ncbi.nlm.nih.gov/pubmed/26947201

4. Roche Internal Clinical Study Report. (Accessed on 26 Jun 2023).

5. Lugtenburg P, Avivi I, Berenschot H, et al. Efficacy and safety of subcutaneous and intravenous rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in first-line diffuse large B-cell lymphoma: the randomized MabEase study. Haematologica 2017;102:1913-1922. https://www.ncbi.nlm.nih.gov/pubmed/28935843

6. Roche Internal Regulatory Document. (Accessed on 26 Jun 2023).