Timing of MabThera Administration with Surgery

This article responds to your request for information on administration timing of MabThera® (rituximab) with surgery. This response was developed according to the principles of evidence-based medicine and contains data from clinical trials .

In brief

- There is limited data and guidance on the safety of surgery in patients who have received rituximab.
- Experts have taken other factors such as B-cell depletion into consideration which is theorized to increase infection and delay healing.
- Roche respects the clinical decision by the healthcare professional (HCP) to appropriately administer perioperative rituximab on a case-by-case basis after outweigh all of the risks and benefits.

Timing of MabThera with surgery in Roche studies

Roche has no recommendations or specific information on when to administer MabThera in relation to surgery. We cannot provide therapeutic recommendation for individual patients.

However, the timing of MabThera administration in relation to surgery was accounted for during enrollment of our clinical studies.

Eligibility criteria in the REFLEX study

The REFLEX study evaluated the long term efficacy and safety of MabThera combined with methotrexate in participants with rheumatoid arthritis who have had an inadequate response to anti-tumor necrossis (TNF) alpha therapy.

The REFLEX study excluded patients with:

- Bone/joint surgery within 8 week prior to screening, including joint fusion.
- Joint surgery planned within 24 weeks of randomization.[1,2]

Timing of MabThera with surgery and safety events reported in the literature

Strangfeld et al. evaluated the frequency of periprosthetic infection in patients treated with conventional disease-modifying antirheumatic drugs (DMARDs), including Mabthera, or biologic agents who had undergone total joint replacement (TJR) of the hip, knee, shoulder, or ankle using the German biologics registry (RABBIT).[3] Of the 229 patients treated with Mabthera (266 patient-years observation), there were no cases of periprosthetic infection observed.

Godot et al. evaluated 133 patients who underwent surgeries within a year after receiving MabThera in RA from the French Society of Rheumatology AutoImmunity and Rituximab (AIR) registry.[4] Median delay between surgery and the last rituximab infusion was 6.4 months. Ninety-four of 140 total procedures

(67%) were orthopedic surgeries in this group of patients. Nine (6.7%) patients experienced 12 (8.5%) complications including

- deep infections (n=6)
- scars or superficial infections at the surgical site (n=2)
- pulmonary infection (n=1)
- delayed healing (n=1)
- deep vein thrombosis (n=1), and
- dead associated with septic shock (n=1).

Multivariate logistic regression analysis of patient characteristics did not reveal predictive factors for complications from surgical procedures

Saech et al. evaluated 13 patients with RA who received MabThera prior to 18 total surgeries.[5] Surgeries were predominately elective orthopedic procedures (14/18). The mean time between MabThera administration and surgery was 6±4 months. Almost all patients showed absent or low levels of peripheral B-cells at the time of surgical procedure. No severe infections were observed. Soft tissue (n=1) and urinary tract infection (n=1) postoperative infections were reported. Wound healing disturbances occured in 3 patients. All events were resolved with IV antibotics and/or appropriate wound management.

Potential effect of B-cell depletion on wound healing

Peripheral B-cell depletion, associated with MabThera treatment, is theorized to increase infection and delay healing.[4] In some patients treated with MabThera for hematological malignancies, B-cell recovery began within 6 months of treatment and generally returned to normal levels within 12 months after completion of rituximab therapy.[6] This may take longer in some other patients (up to median recovery time of 23 months post-induction therapy).

Clinical considerations from professional organizations

The lieu of more data detailing risks evaluated in published studies experts have also taken into consideration

- the nature and potential complication of the surgical procedure
- patient-related factors, such as concomittant medications, comorbidities, and history of infection, and
- the severity of patients' disease and therapeutic need of rituximab to treat the baseline disease.[7]

References

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