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Pharmacotherapeutic report on ofatumumab (Arzerra®) for the indication 'Chronic Lymphatic Leukaemia (CLL) in patients who are refractory for fludarabine and alemtuzumab'

Medicine. Intravenous ofatumumab

Summary of the therapeutic value

Favourable effects. In a single open-label, one-armed, non-randomised study of patients with CLL who were refractory for fludarabine and alemtuzumab, an 58% objective response was found, a median progression-free survival of 5.7 months and a general survival lasting 13.7 months. However, no conclusions could be drawn about the extent of the effect on these patients due to the absence of a comparative treatment. In a retrospective, observational study, in which the same refractory patients were treated with various standard therapies, an 20% objective response was found and a general survival duration of 8 months. In the light of this retrospective comparison, the severity of the disease and the absence of an alternative treatment, the observed effects of this third-line treatment seem relevant.

Unfavourable effects. There is a very high frequency of infections and infusion reactions during treatment with ofatumumab. However, infections are inherent to the often elaborate preliminary treatment of this group of CLL patients, and they are usually unrelated to the treatment with ofatumumab. Other side effects with a very high frequency are coughing, diarrhoea, anaemia, tiredness, fever, neutropenia, dyspnoea, nausea and skin rashes. Reported severe side effects are tumour lysis syndrome, progressive multifocal leukoencephalopathy, febrile neutropenia and severe infusion reactions and infections, including fatal infections.

Based on extrapolation, the side effects profile of ofatumumab seems identical to the side effects profile of another anti-CD20 monoclonal antibody, rituximab. However, the degree and impact of the side effects is unclear due to the lack of a control group in the most important study.

Experience. Ofatumumab is registered as an orphan drug and experience with it is limited.

Applicability. Ofatumumab has a broad applicability, limited only by possible side effects. Based on the limited data available, no dose adjustment is necessary for elderly patients and patients with a reduced renal or liver function.

Ease of use. Ofatumumab is administered by means of an intravenous infusion. The infusion schedule comprises 8 weekly infusions followed by 4 monthly infusions.

Final conclusion. The orphan drug ofatumumab demonstrated a high objective response in patients who are refractory for fludarabine and alemtuzumab. Based on a retrospective comparison, and in view of the severity of the disease and the absence of an alternative treatment, the conclusion is that, in spite of the limited data, ofatumumab has a therapeutic added value in comparison with not using ofatumumab for the treatment of chronic lymphatic leukaemia (CLL) in patients who are refractory for fludarabine and alemtuzumab.

*The original text of the summary of this **CFH-report** was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of the summary of the CFH-report.*
Furthermore, CVZ points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.