

Guidance on the prevention of Listeria infection after alemtuzumab treatment of multiple sclerosis

Summary

- 1. The risk of Listeria meningitis/septicaemia is 0.25% in the first month after each cycle of alemtuzumab treatment.**
- 2. We recommend two preventative approaches, of which the most straightforward is co-trimoxazole 960mg three times a week for one month after each cycle of alemtuzumab (that is, following the same schedule as acyclovir).**
- 3. For patients who will definitely be compliant with the Listeria-free diet an alternative is: eight days of amoxicillin 1g tds or co-trimoxazole 960mg bd to eliminate Listeria colonisation (starting four days before alemtuzumab treatment) followed by the Listeria-free diet for one month after alemtuzumab.**
- 4. Please continue to report cases of Listeria after alemtuzumab so that we can refine this advice.**

Background

- Listeria meningitis was first reported after alemtuzumab in 2008 (Coles NEJM)
- Since the licensing of alemtuzumab in the EU in 2013 and US in 2014, there have been several case reports of Listeria in the days of alemtuzumab treatment (Rau 2015, Holmøy 2017).
- As a result, in 2016 Genzyme Sanofi altered the SPC for alemtuzumab (Lemtrada) to include “Listeriosis/Listeria meningitis has been reported in LEMTRADA treated patients, generally within one month of LEMTRADA infusion. To reduce this risk, patients receiving LEMTRADA should avoid ingestion of uncooked or undercooked meats, soft cheeses and unpasteurized dairy products for at least one month after LEMTRADA treatment.”
- Since marketing authorisation, Genzyme Sanofi pharmacovigilance has been informed of 32 cases of Listeria meningitis/septicaemia. During this time, roughly 13,000 people have received alemtuzumab. Nearly all infections have occurred in the first month after alemtuzumab. As with all post marketing safety reports sent to companies, there is a frustrating lack of detail about these cases, despite outreach by Sanofi Genzyme, and it is not clear if patients were adequately complying with the diet.

Prevention of Listeria post alemtuzumab

David Partridge (Consultant Microbiologist) and David Paling (Consultant Neurologist) advise that Listeria after alemtuzumab is likely to be due to Listeria already colonising the bowel at the time of alemtuzumab treatment. The Listeria-free diet would ideally need to be started

ninety days before treatment to reduce this colonisation and minimise risk of infection development. This is too prolonged for most people receiving the first cycle of alemtuzumab, who may have active multiple sclerosis that needs treating. Furthermore, a majority of the neurologists contributing to this advice were not confident that all people with multiple sclerosis would comply with the Listeria-free diet.

1. So, the consensus was that the safest advice is co-trimoxazole 960mg three times a week for one month.
2. An alternative approach, if the patient will comply rigorously with the Listeria-free diet is one week of amoxicillin 1g tds or co-trimoxazole 960mg bd to eliminate Listeria from the bowel (for instance for 8 days starting the Friday before treatment on the Monday) followed by the Listeria-free diet for one month after alemtuzumab.
3. Finally, where alemtuzumab treatment can be predicted some months in advance (for instance with cycles 2 and 3), it would be reasonable to offer a third option to patients who will comply rigorously with the Listeria-free diet: going on the Listeria-free diet for ninety days before, and for one month after, alemtuzumab.

References

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2: Rau D, Lang M, Harth A, Naumann M, Weber F, Tumani H, Bayas A. Listeria Meningitis Complicating Alemtuzumab Treatment in Multiple Sclerosis--Report of Two Cases. Int J Mol Sci. 2015 Jun 29;16(7):14669-76. doi: 10.3390/ijms160714669. PubMed PMID: 26132570; PubMed Central PMCID: PMC4519865.

3: CAMMS223 Trial Investigators., Coles AJ, Compston DA, Selmaj KW, Lake SL, Moran S, Margolin DH, Norris K, Tandon PK. Alemtuzumab vs. interferon beta-1a in early multiple sclerosis. N Engl J Med. 2008 Oct 23;359(17):1786-801. doi: 10.1056/NEJMoa0802670. PubMed PMID: 18946064.

Lemtrada SPC: <https://www.medicines.org.uk/emc/medicine/28917>

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