Eflornithine (DFMO) in the treatment of high-risk neuroblastoma patients

Information for patients and families

on behalf of
UK Neuroblastoma Clinical Trials Group & CCLG Neuroblastoma Special Interest Group
7 Oct 2024

Eflornithine (Difluoromethylornithine or DFMO) is an oral drug, which has been investigated for its effects in neuroblastoma. In December 2023 it was approved by the FDA (Food and Drug Administration) in the US for patients with high-risk neuroblastoma who have had a response to prior multimodal treatment including anti-GD2 immunotherapy. This approval was mainly based on data comparing[1] a single arm Phase 2 trial study with US frontline treatment on the COG ANBL0032 trial[2].

In the trial, DFMO was given orally for two years after completion of treatment for high-risk neuroblastoma. According to the analysis[3], Four-year Event Free Survival from the end of immunotherapy was 84% in the DFMO group versus 72% in the non-DFMO group. Data from 360 patients was assessed for toxicity and safety; the most common adverse reactions were hearing loss, ear infection, fever, pneumonia, and diarrhoea. New or worsening hearing loss requiring new use of hearing aids occurred in 7% of patients.

There are significant limitations to the data, and ideally a randomised controlled trial (RCT) would have been done some years ago to produce robust scientific evidence. However, due to the existing data and FDA approval, a randomised trial is not now feasible. Data on the efficacy and safety of DFMO added to the end of standard SIOPEN multimodal therapy is lacking.

Following the FDA approval of DFMO, guidelines for treatment of neuroblastoma in the US were updated, with a recommendation[4] that doctors discuss DFMO as a continuation therapy option with patients and families, and it is now being widely prescribed in the US.

In Europe, an application for approval of DFMO use for high-risk neuroblastoma with the MHRA (Medicines and Healthcare products Regulatory Agency) and EMA (The European Medicines Agency) is in progress by the pharmaceutical company, Norgine. In the meantime, on 7th October, Norgine launched an Expanded Access Program (EAP) in the UK, to allow access to DFMO while approval and funding is sought. The program provides free of charge DFMO to patients, via their normal NHS oncology service, on a named patient basis.

In light of the above, SIOPEN, the European Neuroblastoma Research Network, has issued a statement, acknowledging use of DFMO in front-line treatment of high-risk neuroblastoma (Statements — SIOPEN Research Network). The UK Neuroblastoma Clinical Trials Group and CCLG Neuroblastoma Special Interest group suggest that treatment with DFMO for high-risk neuroblastoma patients, is considered and discussed with patients and families who are completing frontline therapy or relapse therapy.

Key information:

- Inclusion criteria for the Expanded Access Program (EAP):
    - Diagnosis of high-risk neuroblastoma
    - Patients have demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy
    - Greater than 30 days from completion of chemotherapy and immunotherapy and **less than 120 days** from previous therapy
    - Patient meets clinical eligibility to receive DFMO in the opinion of their doctor
    - All patients and/or legal guardians must sign informed written consent
    - Patient is resident in the country where the EAP request is made
    - Not eligible for any clinical trials which would provide access to DFMO in patient's country of residence
- Exclusion criteria for the Expanded Access Program (EAP):
    - Patients who are currently receiving another investigational drug are excluded from participation
    - Patients who are currently receiving other anticancer agents are not eligible

- DFMO is available as tablets, which may be swallowed, crushed or chewed.

- During DFMO the following will be monitored:
    - Liver function tests and full blood count before starting to take DFMO and repeated monthly for the first six months of treatment. After six months to be monitored three-monthly or as the clinician advises. More frequent testing will take place in patients whose liver function tests indicate liver function may be affected or who develop low blood counts.
    - Hearing tests before starting to take DFMO and repeated six-monthly during treatment

- If patients have side effects which affect blood counts, liver function or hearing doses of DFMO may be changed or omitted.

This information does not replace any patient information that is supplied by the pharmaceutical company with the drug itself regarding administration, side effects and nutritional guidance.

1. The Event-Free Survival hazard ratio (HR) was 0.48 (95% CI, 0.27 to 0.85) and Overall Survival HR was 0.32 (95% CI, 0.15 to 0.70) in favour of treatment with DFMO compared to no post-maintenance treatment.
2. Oesterheld J, Ferguson W, Kraveka JM, et al. Eflornithine as Postimmunotherapy Maintenance in High-Risk Neuroblastoma: Externally Controlled, Propensity Score-Matched Survival Outcome Comparisons. J Clin Oncol 2024; 42(1): 90-102.
3. Data from 91 patients on the trial was matched to 270 patients who had had the same front-line treatment regime on the COG ANBL0031 trial.
4. Bagatell R, Park JR, Acharya S, et al. Neuroblastoma, Version 2.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw 2024; 22(6): 413-33.