Report COPIKTRA® Duvelisib

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: duvelisib **Brand Name:** Copiktra® **Originator/licensee:** Verastem Europe GmbH **Classification:** NCE **ATC code:** L01EM04 **Orphan Status:** **Eu:** No **Us:** Yes **Mechanism of action:** duvelisib is a PI3K inhibitor with dual activity against the PI3K-δ and PI3K-γ isoforms, involved in the proliferation and survival of malignant B-cell lines and primary CLL tumour cells. [1][2]	**Authorized Indication:** **EMA:** indicated for treatment of adult pts with RR CLL after at least two prior therapies. [1] **FDA:** duvelisib is indicated for the treatment of adult pts with RR CLL or SLL after at least two prior therapies. [2] **Route of administration:** OS **Licensing status:** **EU CHMP P.O. date:** 25/03/2021 **FDA M.A. date:** 24/09/2018 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** Yes --- **ABBREVIATIONS:** **AE:** adverse event **CHMP:** committee for medicinal products for human use **CIT:** chemoimmunotherapy **CLL:** chronic lymphocytic leukaemia **IRC:** independent review committee **M.A.:** marketing authorization **OS:** oral administration **PFS:** progression-free survival **PI3K:** phosphatidylinositol 3-kinase **P.O.:** positive opinion **pts:** patients **RR:** relapsed or refractory **SLL:** small lymphocytic lymphoma **URTI:** upper respiratory tract infection	**Summary of clinical EFFICACY:** Efficacy in RR CLL/SLL is based on the results of DUO (NCT02004522), a phase 3, randomized, open-label trial comparing duvelisib monotherapy with ofatumumab monotherapy in adult pts with RR CLL (n=312) or SLL (n=7) after at least one prior therapy. Pts were randomized 1:1 to oral duvelisib 25 mg twice daily (n=160) or ofatumumab IV (n=159). The primary endpoint was PFS as determined by IRC. Pts in the duvelisib arm had a median PFS of 13.3 months (95% CI: 12.1, 16.8) whereas pts in the ofatumumab arm had a median PFS of 9.9 months (95% CI: 9.2, 11.3), with a HR of 0.52 (95% CI: 0.39, 0.70; p<0.0001). [3][4] **Summary of clinical SAFETY:** Nearly all pts in both arms experienced an AE. The most common AEs were diarrhoea (51% vs 12% in the ofatumumab group), neutropenia (33% vs 21%), pyrexia (29% vs 10%), nausea (23% vs 11%), anemia (23% vs 10%) and cough (21% vs 14%). AEs ≥grade 3 occurred in 87% of duvelisib arm pts and 48% of ofatumumab arm pts. In the duvelisib arm, the most common severe events were neutropenia (30%), diarrhoea (15%), pneumonia (14%) and anemia (13%). Infectious AEs were more frequently reported in the duvelisib arm (69% vs 43%) with pneumonia (18%) and URTI (16%) representing the most common events. Pneumonia was the most frequently reported serious AE in both treatment arms (duvelisib 15% vs ofatumumab 3%). 55 pts (35%) discontinued duvelisib because of AEs. There were 19 fatal AEs (12%) on the duvelisib arm, four of which were assessed by investigators as related to study drug. On the ofatumumab arm, seven pts (5%) had fatal AEs, although none were attributed to ofatumumab treatment. [3] **Ongoing studies:** • ***For the same indication:*** Yes • ***For other indications:*** Yes **Discontinued studies (for the same indication):** Yes --- **References:** 1. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/copiktra 2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/211155s000lbl.pdf 3. Flinn IW, Hillmen P, et al.: The phase 3 DUO trial: duvelisib vs ofatumumab in relapsed and refractory CLL/SLL. Blood. 2018; 132(23): 2446-2455 4.https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/211155Orig1Orig2s000MultidisciplineR.pdf 5. https://www.osservatoriomalattierare.it/i-tumori-rari/leucemia-linfatica-cronica 6.https://www.annalsofoncology.org/article/S0923-7534(20)42469-X/pdf 7. https://www.ema.europa.eu/en/documents/public-statement/public-statement-arzerra-withdrawal-marketing-authorisation-european-union_en.pdf 8. https://adisinsight.springer.com/drugs/800035173 9.https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=Duvelisib&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 10.https://clinicaltrials.gov/ct2/results?cond=Chronic+Lymphocytic+Leukemia&term=&cntry=&state=&city=&dist=&recrs=a&recrs=b&recrs=d&recrs=e&recrs=f&phase=2	**Cost of Therapy:** not available. **Epidemiology:** CLL is the most common leukaemia in the Western world, with an annual incidence of 2-6/100˙000. The incidence increases to 12.8/100˙000/year at the age of 65, the median age of diagnosis. [5] --- **POSSIBLE PLACE IN THERAPY** The treatment regimens recommended for RR CLL are: -venetoclax+rituximab for 24 months -ibrutinib or acalabrutinib as continuous therapy -idelalisib+rituximab -CIT. [6] In 2019 the M.A. for Arzerra® (ofatumumab) has been withdrawn in the EU at the request of the M.A. holder (commercial reasons). [7] **OTHER INDICATIONS IN DEVELOPMENT:** Non-Hodgkin's lymphoma, hematological malignancies, peripheral T-cell lymphoma. [8][9] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION** Ublituximab, zanubrutinib, dinaciclib, orelabrutinib, umbralisib, pirtobrutinib. [8][10] *Service reorganization: No *Possible off label use: Yes