

Ocrelizumab and malignancies

Overview



Clinical trials

- In clinical trials over 10 years studying regular, 6-monthly dosing of OCR, there has been no increased risk of malignancy and female breast cancer with OCR compared with matched reference MS and general populations¹⁻³



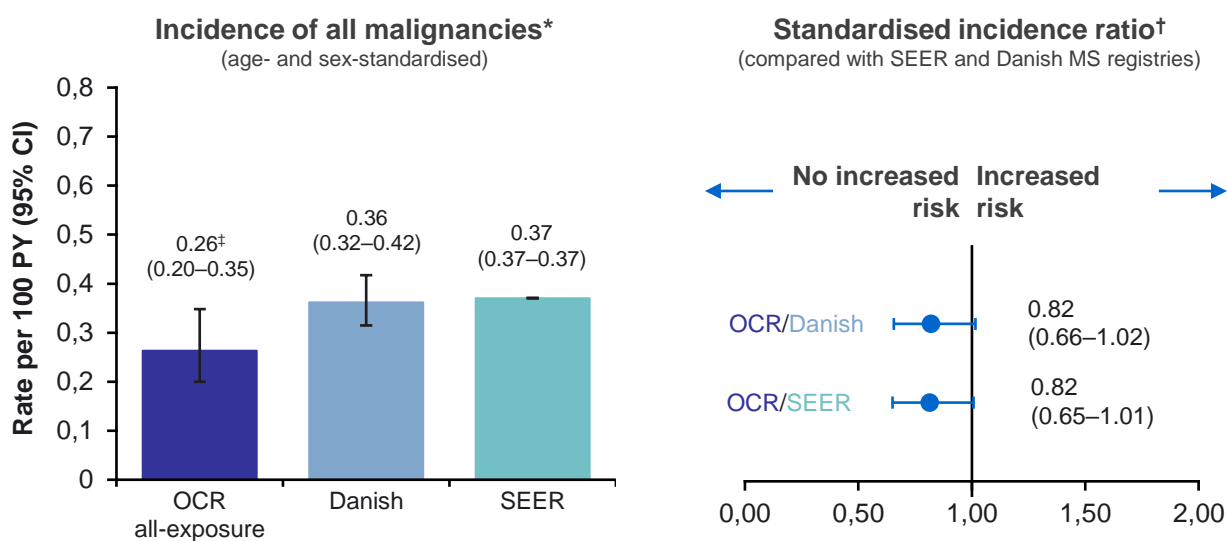
Yearly incidence rates

- Cumulative standardised incidence rates of all malignancies and female breast cancer remained within the range reported in registries²⁻⁴

Clinical trials (ocrelizumab all-exposure population)

Figure 1: Standardised incidence rates per 100 PY of all malignancies (A) and female breast cancer (B)²

A. Incidence of all malignancies (age- and sex-standardised)



B. Incidence of female breast cancer (age-standardised)

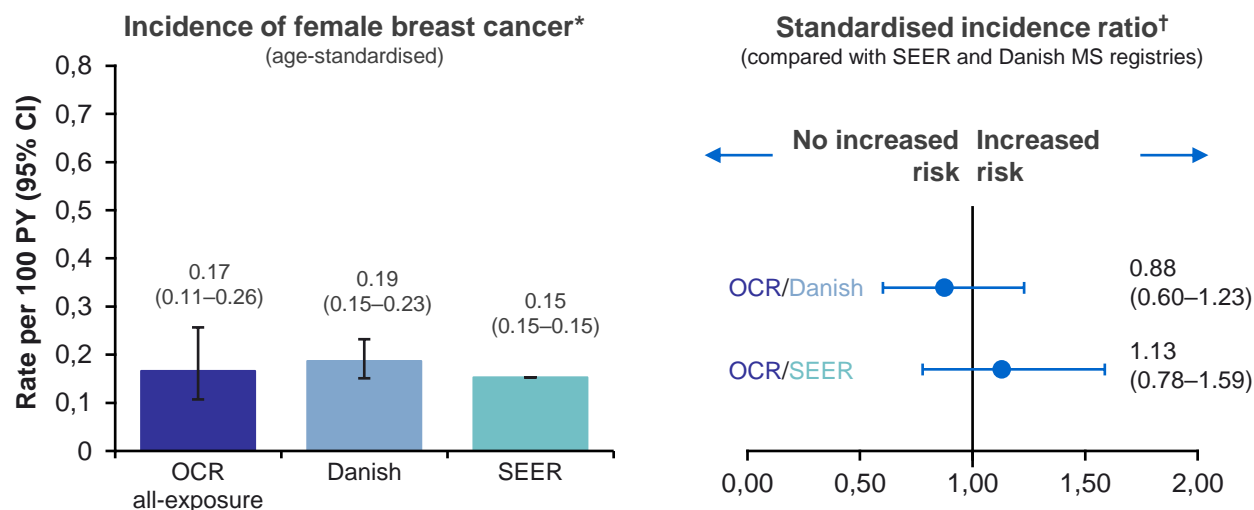
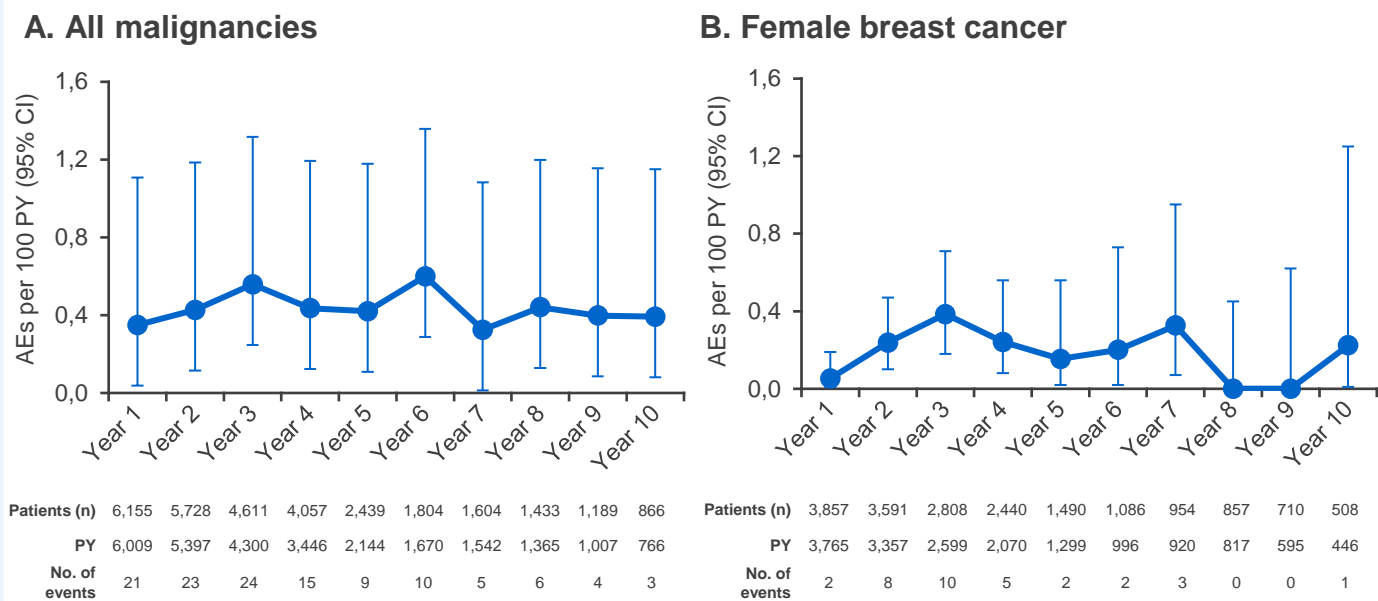


Figure 2: Yearly incidence rates of all malignancies (A) and female breast cancer (B) in the ocrelizumab all-exposure population^{*,2}



Post-marketing experience^{*,5}

As of February 2022:



A total of 162,778 female patients with RMS and PPMS had started OCR globally outside of RCTs



Corresponding to an exposure of 331,539 PY



Overall, 396 cases reporting breast cancer were received, resulting in a crude incidence rate of 0.119 per 100 PYs

Footnotes

Figure 1 (A&B)

*The standardised incidence rates were reported to allow comparison with the SEER database and the Danish MS Registry, using the direct standardisation method. Standardised incidence rates were derived by applying age–sex specific rates to the 2,000 USA standard population, with restriction to the age range of the MS clinical trials (15–59 years);

†The SIR, calculated as observed/expected number of events, was determined for all malignancies (excluding NMSC) and female breast cancer, using the SEER database and the Danish MS Registry as reference populations;

‡It excludes NMSC for comparison with SEER rates, as NMSC is not reported in SEER.

Footnotes (cont.)

Figure 2

*Includes patients who received any dose of OCR during the CTP and associated OLE periods of the Phase II and Phase III studies, plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, CONSONANCE and OLERO, including patients originally randomised to comparator (IFN β -1a or placebo) who switched to open-label OCR treatment. Data cut-off: November 2022. Studies are ongoing.

Post-marketing

*There are well-recognised limitations that should be considered when interpreting spontaneous post-marketing safety reports, including events that may not be causally related to drug exposure; in the real-world setting, events are frequently confounded by factors such as multiple drug use and the presence of pre-existing comorbidities; reporting bias may exist for more significant outcomes, which may result in an overrepresentation of the more serious outcomes; and reporting rates can be stimulated by external factors, such as press reports.

The causes of malignancies are recorded as reported to the company; while the company follows up on all reports to identify the cause, an exact diagnosis is not always possible. Some of the investigations remain ongoing and, therefore, the information may be subject to change.

Exposure was obtained from the PBRER Report 1113817 27 March, 2022. PY have been extrapolated from the female to total Ocrevus patients.

Case counts from the safety data base had reported at least one of the following AE terms. Breast cancer, Invasive papillary breast carcinoma, Invasive ductal breast carcinoma, Breast cancer female, HER2 positive breast cancer, Intraductal proliferative breast lesion, Breast cancer recurrent, Breast cancer stage I, Breast cancer stage II, Invasive breast carcinoma, Breast cancer in situ, Breast cancer metastatic, Breast cancer stage III, Breast cancer stage IV, Breast neoplasm, Hormone receptor positive breast cancer, Invasive lobular breast carcinoma, Lobular breast carcinoma in situ, Triple negative breast cancer.

Abbreviations

AE, adverse event; CI, confidence interval; CTP, controlled treatment period; HER2, human epidermal growth factor receptor 2; IFN β -1a, interferon beta-1a; NIS, non-interventional studies; NMSC, non-melanoma skin cancer; OCR, ocrelizumab; OLE, open-label extension; PBRER, periodic benefit risk evaluation reports; PPMS, primary progressive MS; PY, patient-years; RCT, randomised controlled trial; RMS, relapsing MS; SEER, Surveillance, Epidemiology, and End Results Program; SIR, standardised incidence rate.

References

1. Hauser SL, et al. *Neurology* 2021;97:e1546–59;
2. Hauser SL, et al. Presented at ECTRIMS 2023 (Poster P304);
3. Nørgaard M, et al. *Mult Scler Relat Disord* 2019;28:81–5;
4. National Institutes of Health (NIH). Available at: <https://seer.cancer.gov>. Accessed 13 December, 2023;
5. Roche data on file.