Ocrelizumab and Malignancies

Overview

Clinical trials

- In clinical trials (including open-label extensions) over 10 years studying regular, 6-monthly dosing of OCR, there has been no observed increased risk of malignancy and female breast cancer compared with matched reference MS and general populations[1–3]

Yearly incidence rates

- Cumulative standardized incidence rates of all malignancies and female breast cancer remained within the range reported in registries[2–4]

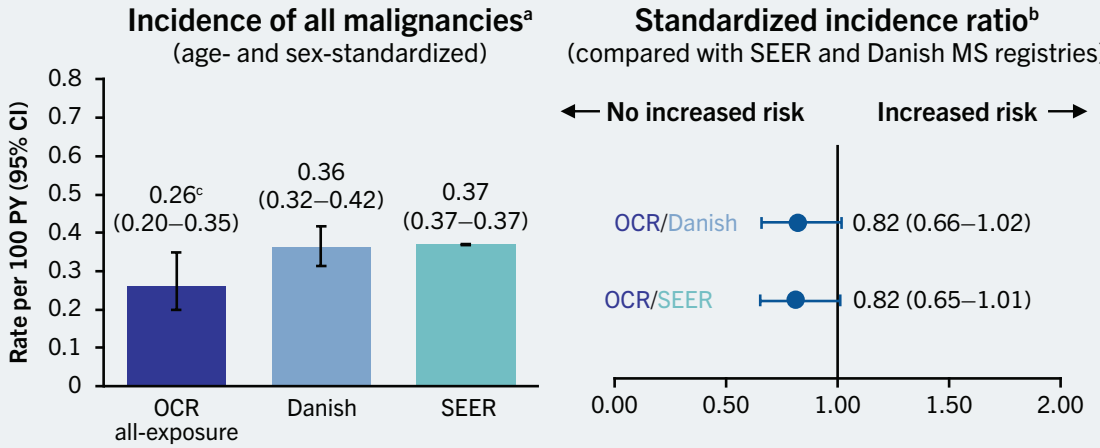
Post-marketing

- The safety profile of OCR continues to be characterized through ongoing clinical trials, post-marketing requirements (PMRs), and post-approval safety studies (PASS), including spontaneous reports to the Roche safety database

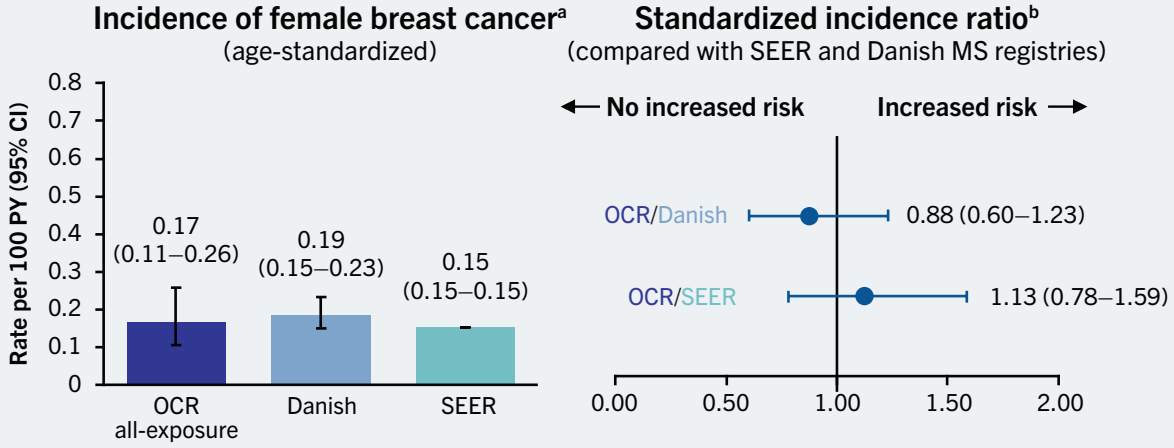
Clinical Trials (Ocrelizumab All-Exposure Population)

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

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

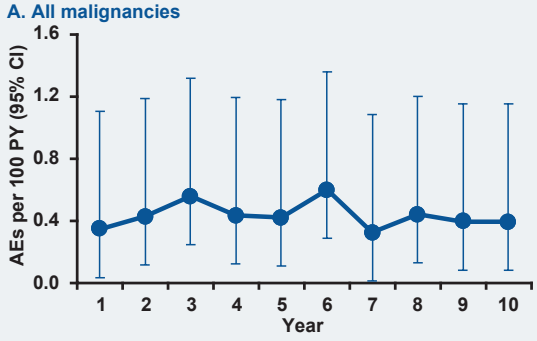


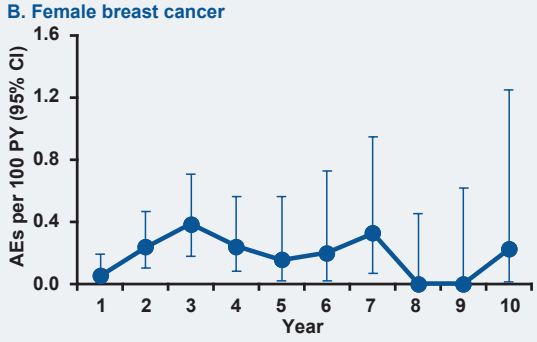
B. Incidence of female breast cancer (age-standardized)



[a]The standardized incidence rates were reported to allow comparison with the SEER database and the Danish MS Registry, using the direct standardization method. Standardized incidence rates were derived by applying age–sex specific rates to the 2000 USA standard population, with restriction to the age range of the MS clinical trials (15–59 years). [b]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. [c]Excludes NMSC for comparison with SEER rates, as NMSC is not reported in SEER.

Figure 2: Yearly incidence rates of all malignancies (A) and female breast cancer (B) in the ocrelizumab all-exposure population[2a]





Patients (n)	6155	5728	4611	4057	2439	1804	1604	1433	1189	866
PY	6009	5397	4300	3446	2144	1670	1542	1365	1007	766
No. of events	21	23	24	15	9	10	5	6	4	3

Patients (n)	3857	3591	2808	2440	1490	1086	954	857	710	508
PY	3765	3357	2599	2070	1299	996	920	817	595	446
No. of events	2	8	10	5	2	2	3	0	0	1

[a]Includes patients who received any dose of OCR during the CTP and associated OLE periods of the phase 2 and phase 3 studies, plus VELOCE, CHORDS, CASTING, OBOE, ENSEMBLE, LIBERTO, CONSONANCE, and OLERO, including patients originally randomized to comparator (IFN β-1a or placebo) who switched to open-label OCR treatment. Data cut-off: November 2022. Studies are ongoing.
The incidence rates of malignancies are derived from varied sources and intended to provide context. Confounding factors that may influence incidence rates have not been accounted for, and therefore, no direct comparisons should be made. Such factors may include, but are not limited to: type of MS, disease duration, risk factors, geographical region, population size, drug exposure, comorbid conditions, treatment history, and duration of follow-up.

Post-Marketing Experience[5a]

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

[a]There are well-recognized 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, March 27, 2022. PY have been extrapolated from the female to total OCREVUS® (ocrelizumab) patients. Case counts from the safety database 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.

The Prescribing Information is the primary source of information on the known and potential risks associated with ocrelizumab.

Abbreviations:
AE=adverse event; CTP=controlled treatment period; HER2=human epidermal growth factor receptor 2; IFN β-1a=interferon beta-1a; MS=multiple sclerosis; NMSC=non-melanoma skin cancer; no=number; OCR=ocrelizumab; OLE=open-label extension; PBRER=periodic benefit risk evaluation reports; PPMS=primary progressive MS; PY=patient-year; RCT=randomized controlled trial; RMS=relapsing multiple sclerosis; SEER=Surveillance, Epidemiology, and End Results Program; SIR=standardized incidence rate; USA=United States of America.

References:
1. Hauser SL, et al. *Neurology.* 2021;97:e1546–e1559. 2. Hauser SL, et al. Presented at: ECTRIMS-ACTRIMS 2023. October 11-13, 2023. Milan, Italy. Poster P304.
3. Nørgaard M, et al. *Mult Scler Relat Disord.* 2019;28:81–85. 4. National Institutes of Health (NIH). Available at: https://seer.cancer.gov. Accessed December 13, 2023.
5. Genentech. Data on file.

Date of preparation: March 2024

https://www.genentech-medinfo.com/our-products/neuroscience/ocrevus.html

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