Ocrelizumab and malignancies

Overview[1]

Standardised incidence rates

- In clinical trials over 8 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 populations[1–4]

Yearly incidence rates

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

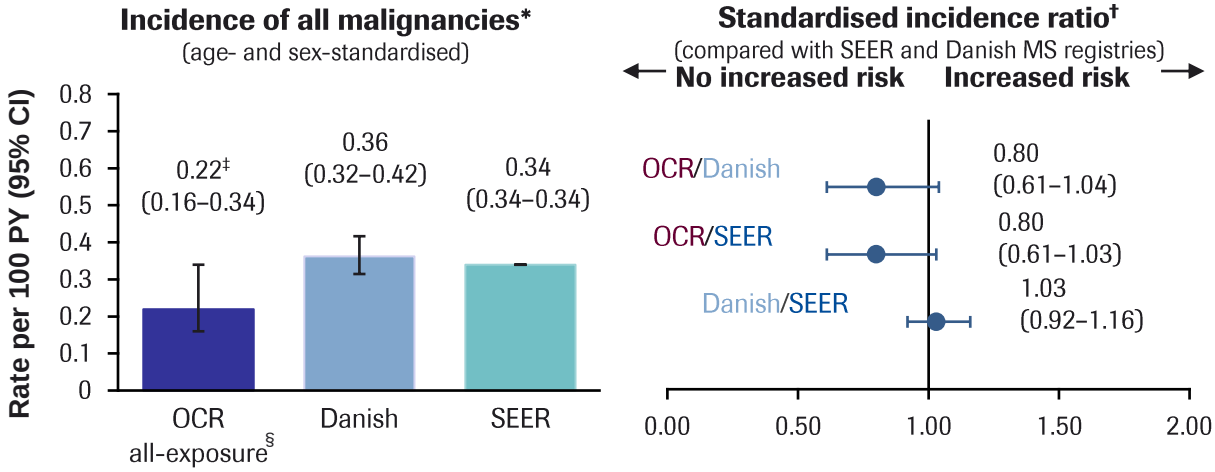
Post-marketing

- The safety profile of OCR continues to be characterised through the ongoing CTs, post-marketing commitment registries (NIS) and post-marketing data, including routine pharmacovigilance

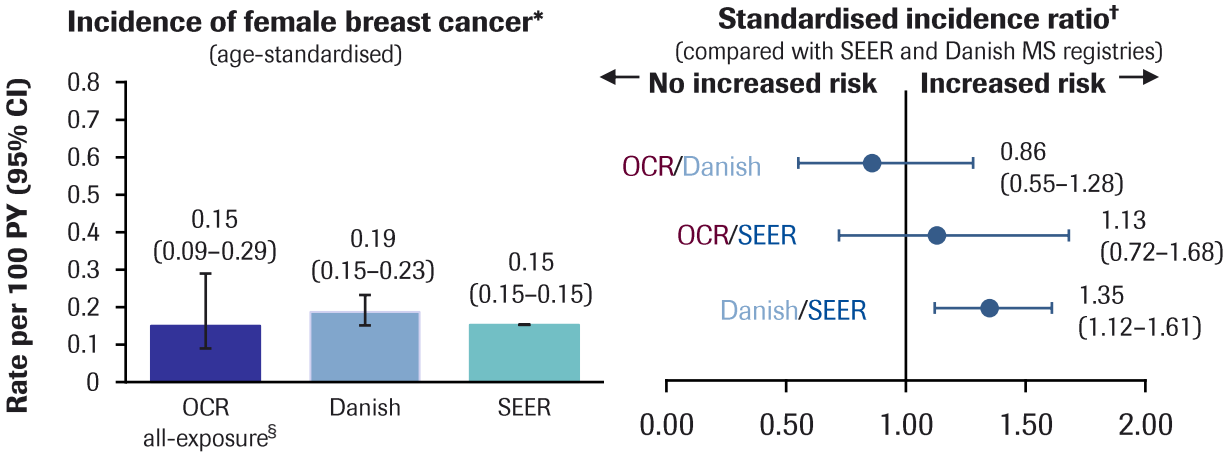
Clinical trials (ocrelizumab all-exposure population)

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)

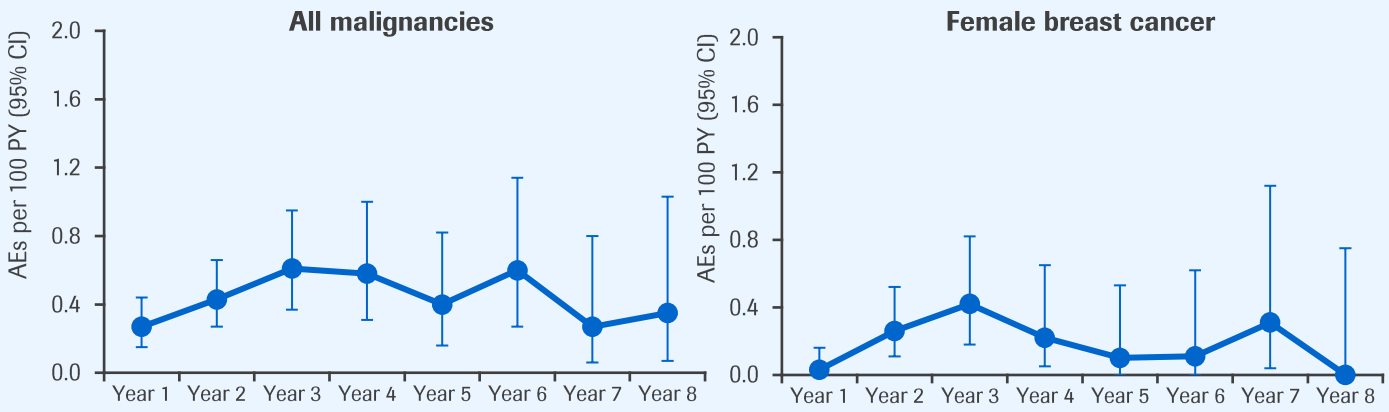


B. Incidence of female breast cancer (Age-standardised)



M-XX-00007056 (Date of preparation: October 2021)
www.ocrelizumabinfo.global

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



	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
n	5,688	5,491	3,596	2,573	1,882	1,595	1,277	955
PY	5,598	4,891	3,130	2,229	1,760	1,501	1,102	851
Events	15	21	19	13	7	9	3	3

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8
n	3,557	3,429	2,235	1,576	1,129	959	753	555
PY	3,497	3,056	1,930	1,346	1,054	902	648	495
Events	1	8	8	3	1	1	2	0

Post-marketing experience*,[5]

As of February 2020:

A total of 57,267 female patients with RMS and PPMS had started OCR in the USA outside of RCTs

Corresponding to an exposure of 79,423 PY

Overall, 98 cases reporting breast cancer were received, resulting in a crude incidence rate of 0.123

Footnotes

Figure 1 (A&B)

*The standardised incidence rates were reported to allow comparison with the SEER database and the Danish MS Registry, usingthe direct standardisation method. Standardised 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);

†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;

§OCR all-exposure population.

M-XX-00007056 (Date of preparation: October 2021)
www.ocrelizumabinfo.global

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 and CONSONANCE, including patients originally randomised to comparator (IFN β-1a or placebo) who switched to open-label OCR treatment. Data cut-off: November 2020. Studies are ongoing.

The incidence rates of serious 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

*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.

Abbreviations

AE, adverse event; CTP, controlled treatment period; IFN β-1a, interferon beta-1a; MedDRA, Medical Dictionary for Regulatory Activities; NIS, non-interventional studies; NMSC, non-melanoma skin cancer; OCR, ocrelizumab; OLE, open-label extension; PPMS, primary progressive MS; pwMS, people with 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;doi:10.1212/WNL.0000000000012700;
2. Hauser SL, *et al.* Presented at ECTRIMS 2021 (Poster P724);
3. Nørgaard M, *et al. Mult Scler Relat Disord* 2019;28:81–5;
4. National Institutes of Health (NIH). Overview of the SEER Program. https://seer.cancer.gov/about/overview.html. Accessed 14 October, 2021;
5. Roche data on file.