Ocrelizumab and malignancies

Overview[1]

Standardised incidence rates

- In clinical trials over 9 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

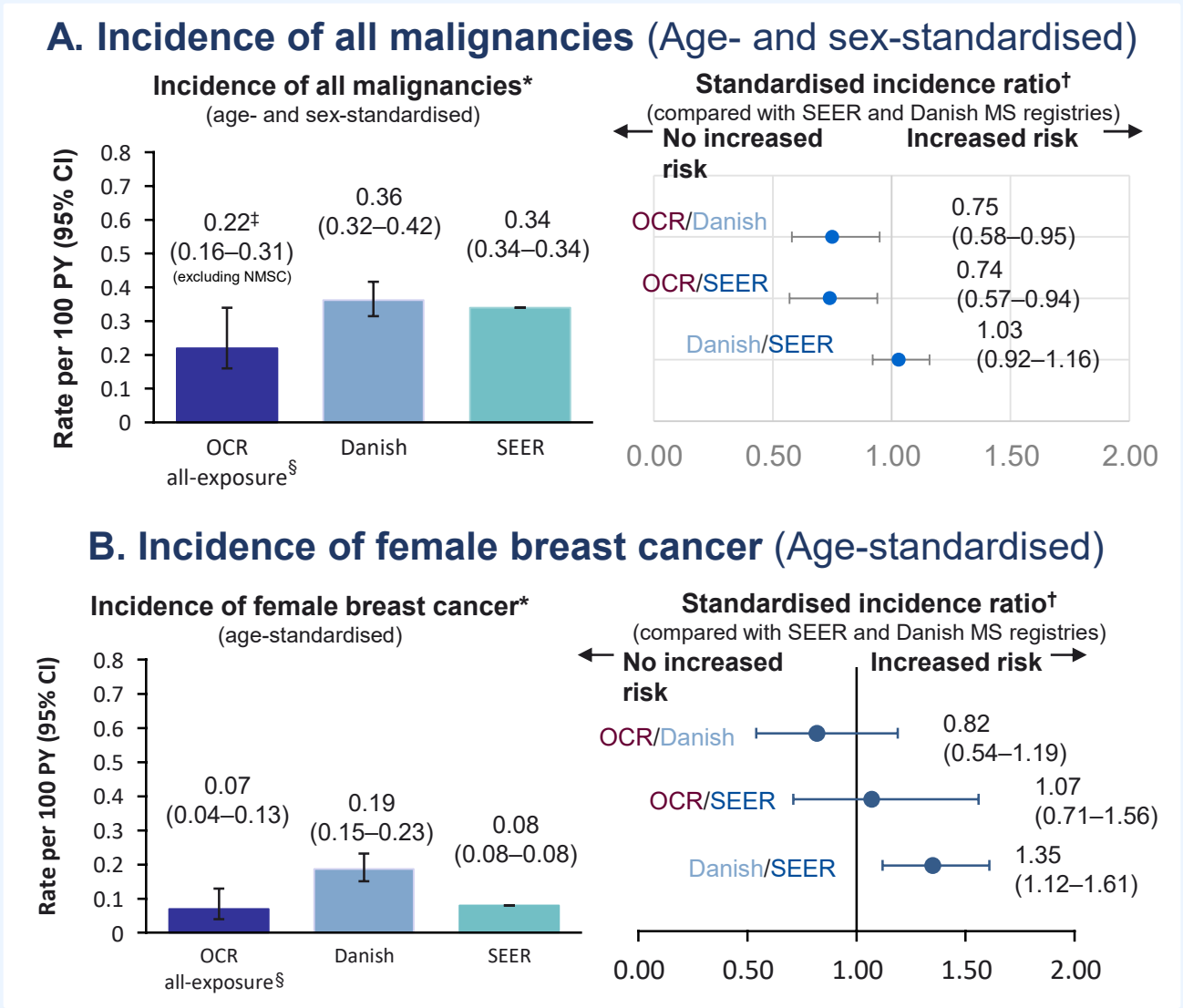
- Cumulative standardised incidence rates of all malignancies and female breast cancer remained within the range reported in registries

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

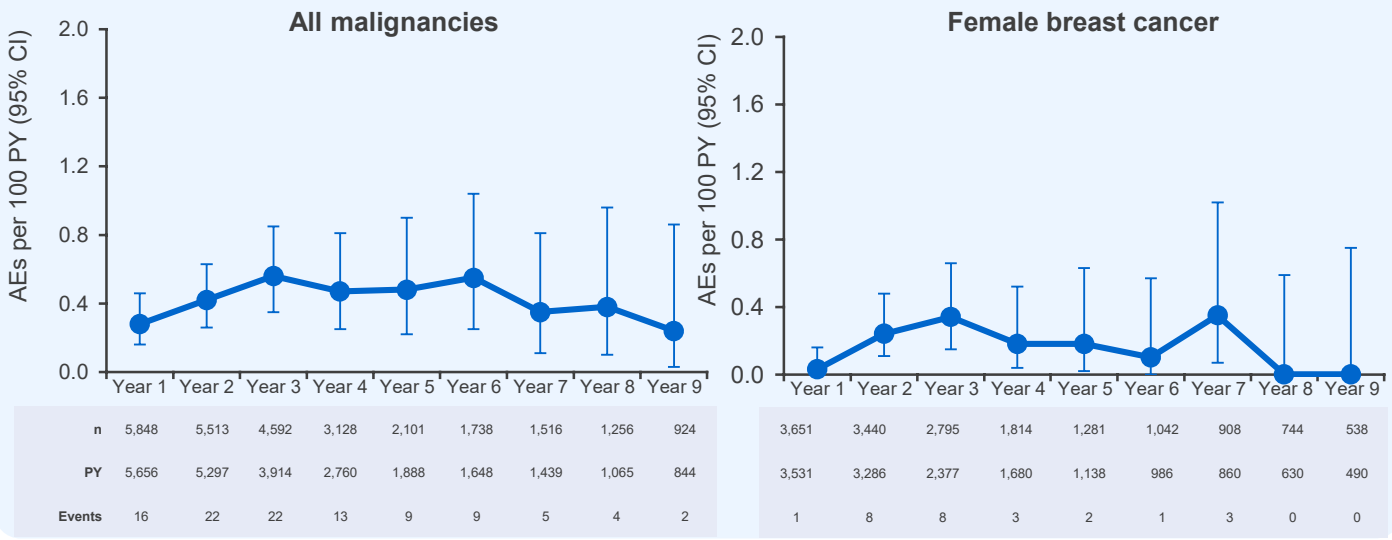
Clinical trials (ocrelizumab all-exposure population)

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



M-XX-00012232 (Date of preparation: January 2023)
www.ocrelizumabinfo.global

Figure 2: 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	Year 9
n	5,848	5,513	4,592	3,128	2,101	1,738	1,516	1,256	924
PY	5,656	5,297	3,914	2,760	1,888	1,648	1,439	1,065	844
Events	16	22	22	13	9	9	5	4	2

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9
n	3,651	3,440	2,795	1,814	1,281	1,042	908	744	538
PY	3,531	3,286	2,377	1,680	1,138	986	860	630	490
Events	1	8	8	3	2	1	3	0	0

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;

§OCR all-exposure population.

M-XX-00012232 (Date of preparation: January 2023)
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 2021. 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.

Exposure was obtained from the PBRER Report 1113817 27 March 2022. Patient Years 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;doi:10.1212/WNL.0000000000012700;
2. Hauser SL, *et al.* Presented at ECTRIMS 2022 (Poster P326);
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;
5. Roche data on file.