FDA Briefing Document

Addendum

BLA 761176

Drug name: ^{131}I-omburtamab

Applicant: Y-mAbs Therapeutics, Incorporated

Oncologic Drugs Advisory Committee Meeting

October 28, 2022

Division of Oncology 2/Office of Oncologic Diseases

DISCLAIMER STATEMENT

The attached package contains background information prepared by the Food and Drug Administration (FDA) for the panel members of the Advisory Committee. The FDA background package often contains assessments and/or conclusions and recommendations written by individual FDA reviewers. Such conclusions and recommendations do not necessarily represent the final position of the individual reviewers, nor do they necessarily represent the final position of the Review Division or Office. We have brought the assessment of the evidence of effectiveness for ^{131}I-omburtamab to this Advisory Committee in order to gain the Committee's insights and opinions, and the background package may not include all issues relevant to the final regulatory recommendation and instead is intended to focus on issues identified by the Agency for discussion by the Advisory Committee. The FDA will not issue a final determination on the issues at hand until input from the Advisory Committee process has been considered and all reviews have been finalized. The final determination may be affected by issues not discussed at the Advisory Committee meeting.

The following analyses represent data from Study 03-133 and CGCCR data with analyses limited to patients in Modality Group 2 (patients who received radiation therapy and one other modality of therapy [surgery or chemotherapy]) and patients with complete case data to better reflect the primary analysis population.

Addendum Table 1: Modality Groups in Study 03-133 and the CGCCR External Control Comparator with complete case data

Group	Treatment Modalities	Study 03-133 (n=94)	External Control (n=120)
Group 1	Received at least one post-relapse therapy	84 (89%)	74 (62%)
Group 2	Received post-relapse radiation therapy and at least one other therapy (surgery or chemo)	77 (82%)	34 (28%)
Group 3	Received post-relapse radiation therapy, surgery, and chemotherapy	63 (67%)	21 (18%)

Addendum Table 2: Comparison of post-CNS relapse CNS-directed radiation therapy in Study 03-133 and External Control patients in Modality Group 2 with complete case data

Study 03-133 (n=77)	External Control (n=34)
Median time from relapse to first RT was 21 days (3, 266)	Median time from relapse to first RT was 69 days (3, 414)
95% of patients received craniospinal irradiation 18 or 21 Gy +/- boost	No patient received craniospinal irradiation No further details on type/dose of RT available

Addendum Table 3: Comparison of post-CNS relapse chemotherapy in Study 03-133 and External Control patients in Modality Group 2 with complete case data

Study 03-133 (n=77)	External Control (n=34)
99% received chemotherapy post-relapse, prior to omburtamab	88% received chemotherapy post-relapse
Most patients received temozolomide/irinotecan	Most patients received topotecan/etoposide No patients reported to have received temozolomide or irinotecan

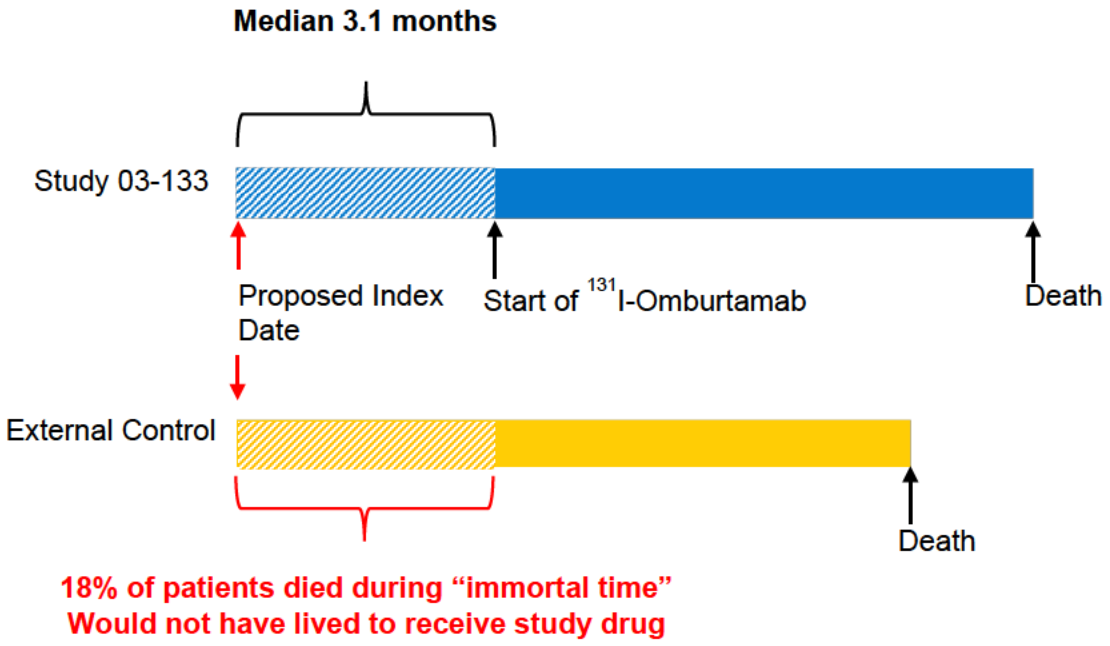
Addendum Table 4: Survival in CGCCR external control based on modality grouping in patients with complete case data

Group	Treatment Modalities	External Control (n=120)	
		Number of Patients	Median OS* (months)
Group 1	Received at least one post-relapse therapy	74	10.0 (95% CI: 6.9, 15.2)
Group 2	**Received post-relapse radiation therapy and at least one other therapy (surgery or chemo)**	**34**	**16.6** **(95% CI: 9.8, 31.3)**
Group 3	Received post-relapse radiation therapy, surgery, and chemotherapy	21	29.8 (95% CI: 11.7, NE)

Addendum Table 5: Survival in CGCCR external control based on era of therapy in patients with complete case data in Modality Group 2

Era of Therapy	External Control (n=34)	
	Number of Patients	Median OS* (months)
Before Trial 03-133 (1990-2005)	17	11.4 (95% CI: 6.8, 17.9)
Contemporaneous (2005-present)**	17	31.3 (95% CI: 10.0, NE)

Addendum Figure 1: Immortal Time Bias (Credited Survival) Related to Index Date Selection.



The median time between Applicant's proposed index date (Index Date A) and the start of ^{131}I-omburtamab (Index Date D)(Immortal Time) was 3.1 months (range 0.6 to 24.9 months) in patients in Study 03-133 in Modality Group 2 with complete case data. In the external control, among 34 patients who received post-CNS relapse radiation therapy and at least one additional modality of therapy (surgery or chemotherapy), 6 patients (18%) died within 3.1 months of Index Date A. This subset may represent patients who would have been excluded from eligibility for Study 03-133 due to immortal time bias, had they otherwise had an opportunity to enroll.