Oncologic Drugs Advisory Committee (ODAC) Meeting

July 25, 2024

BLA# 761069/Supplement 43

Drug name: durvalumab

Applicant: AstraZeneca UK Limited

ADVISORY COMMITTEE BRIEFING MATERIALS: AVAILABLE FOR PUBLIC RELEASE

ERRATA

To the Combined FDA and Applicant ODAC Briefing Document

Errata to the Briefing Document:

Background from the Applicant:

The Applicant would like to provide correction to Table 8, page 40 in the combined ODAC Briefing Document. The original table is shown below followed by a table with corrections in red. The conclusions remain unchanged.

Of note, two patients in the D + CTx arm with an adverse event with outcome of death [interstitial lung disease and aortic aneurysm rupture (one patient each)] were captured in both the post-surgery and adjuvant periods. Given the definitions of the surgical period and the adjuvant period (see footnotes in Table 8 below), these periods may potentially overlap.

Original table, page 40 in the combined ODAC Briefing Document:

Table 8 Overview of adverse events by category and by study treatment period (SAS population; Safety Update DCO)

N (%)	Neoadjuvant period †		Surgical period ‡		Adjuvant period §		Overall ¶		Pooled D Safety Data (N = 4045)
	D + CTx (N = 401)	Pbo CTx (N = 398)	D + CTx (N = 325)	Pbo CTx (N = 326)	D + CTx (N = 266)	Pbo + CTx (N = 254)	D + CTx (N = 401)	Pbo + CTx (N = 398)	
Any-Grade all-causality AEs	**365 (91.0)**	**357 (89.7)**	**235 (72.3)**	**219 (67.2)**	**223 (83.8)**	**190 (74.8)**	**387 (96.5)**	**379 (95.2)**	**3825 (94.6)**
Max. CTCAE Grade 3 or 4	130 (32.4)	145 (36.4)	55 (16.9)	41 (12.6)	41 (15.4)	27 (10.6)	174 (43.4)	172 (43.2)	1600 (39.6)
SAEs	83 (20.7)	66 (16.6)	61(18.8)	51 (15.6)	40 (15.0)	26 (10.2)	156 (38.9)	126 (31.7)	1447 (35.8)
Outcome of **death**	8 (2.0)	4 (1.0)	11 (3.4)	9 (2.8)	4 (1.5)	2 (0.8)	23 (5.7)	15 (3.8)	231 (5.7)
AEs Leading to discontinuation of Any Treatment	54 (13.5)	31 (7.8)	N/A	N/A	26 (9.8)	10 (3.9)	78 (19.5)	40 (10.1)	397 (9.8)
AEs leading to discontinuation of D/Pbo	26 (6.5)	15(3.8)	2(0.6)	2(0.6)	26(9.8)	10(3.9)	51 (12.7)	25(6.3)	397 (9.8)
AEs leading to discontinuation of CTx	48(12.8)	31(7.8)	N/A	N/A	N/A	N/A	48(12.0)	31(7.8)	N/A
AEs leading to discontinuation of both D/Pbo and CTx	20(5.0)	15(3.8)	N/A	N/A	N/A	N/A	20(5.0)	15(3.8)	N/A
AEs Leading to on-study surgery not done	7 (1.7)	4 (1.0)	N/A	N/A	N/A	N/A	7 (1.7)	4 (1.0)	N/A
Any-Grade AEs possibly related to any study treatment	**330 (82.3)**	**313 (78.6)**	**83 (25.5)**	**36 (11.0)**	**128 (48.1)**	**74 (29.1)**	**350 (87.3)**	**325 (81.7)**	**2340 (57.8)**
Max. Grade 3 or 4	117 (29.2)	129 (32.4)	11 (3.4)	3 (0.9)	20 (7.5)	9 (3.5)	133 (33.2)	132 (33.2)	459 (11.3)
Outcome of death	3 (0.7)	1 (0.3)	3 (0.9)	0	1 (0.4)	1 (0.4)	7 (1.7)	2 (0.5)	27 (0.7)
Any-Grade imAEs #	33 (8.2)	19 (4.8)	19 (5.8)	2 (0.6)	60 (22.6)	20 (7.9)	102 (25.4)	40 (10.1)	705 (17.4)
imAEs Max. CTCAE Grade 3-4	6 (1.5)	5 (1.3)	6 (1.8)	1 (0.3)	6 (2.3)	4 (1.6)	18 (4.5)	10 (2.5)	175 (4.3)

† First dose of Study Tx (D/Pbo/CT) until the date of surgery or, for patients without surgery, up to the earliest of: last dose of neoadjuvant Tx (D/Pbo/CT) + 90 days, first dose of subsequent anti-cancer Tx, or the DCO date; for assessments recorded on the day of surgery, time was used to determine if it was pre- or post-surgery (if time was not available, it was assumed to occur post-surgery). ‡ Date of surgery (inclusive) to the earliest of 90 days post-surgery, first dose of subsequent anti-cancer Tx, or DCO date. § Date of first dose of Study Tx post-surgery until earliest of: last Study Tx post-surgery + 90 days, date of first dose of subsequent anti-cancer Tx, or DCO date. ¶ First dose of Study Tx (D/Pbo/CT) until the earliest of: the last dose of Study Tx or surgery (taking the latest dose of D/Pbo/CTx/date of surgery) + 90 days, date of the first dose of subsequent anti-cancer Tx, or DCO date. # An AE of special interest consistent with an immune-mediated mechanism of action, where there is no clear alternate etiology, and requiring the use of systemic corticosteroids or other immunosuppressants and/or, for specific endocrine events, endocrine therapy. One patient assigned to the Pbo arm erroneously received a single cycle of D (in the adjuvant phase) and was included in the D arm for the safety analyses.

All reported percentages are based on the total number of patients in each column header as the denominator (i.e., patients who received Tx during that period).
Source: Table 14.3.6.2.1.1.120DSU, iemt 0617.21, iemt 0617.69, Table 14.3.6.2.1.120DSU, Table 14.3.2.1.4.120DSU, Table 14.3.6.2.1.1.120DSU, Table 14.3.2.1.1.120DSU, Table 14.3.2.1.3.120DSU, iemt0617_021, iemt0617.108, Table 14.3.2.2.2.120DSU and Table 14.3.4.1.1.2.120DSU

The table has been corrected as:

Table 8 Overview of adverse events by category and by study treatment period (SAS population; DCO4)

N (%)	Neoadjuvant period †		Surgical period ‡		Adjuvant period §		Overall ¶		Pooled D Safety Data (N = 4045)
	D + CTx (N = 401)	Pbo CTx (N = 398)	D + CTx (N = 325)	Pbo + CTx (N = 326)	D + CTx (N = 266)	Pbo + CTx (N = 254)	D + CTx (N = 401)	Pbo + CTx (N = 398)	
Any-Grade any causality AEs	**365 (91.0)**	**357 (89.7)**	**239 (73.5)**	**227 (69.6)**	**224 (84.2)**	**195 (76.8)**	**387 (96.5)**	**379 (95.2)**	**3825 (94.6)**
AEs of max. CTCAE Grade 3 or 4	131 (32.7)	145 (36.4)	56 (17.2)	43 (13.2)	41 (15.4)	27 (10.6)	175 (43.6)	172 (43.2)	1600 (39.6)
SAEs	83 (20.7)	66 (16.6)	61 (18.8)	51 (15.6)	41 (15.4)	26 (10.2)	157 (39.2)	126 (31.7)	1447 (35.8)
AEs with outcome of death	**8 (2.0)**	**4 (1.0)**	**13 (4.0)**	**9 (2.8)**	**4 (1.5)**	**2 (0.8)**	**23 (5.7)**	**15 (3.8)**	**231 (5.7)**
AEs Leading to discontinuation of any study treatment	54 (13.5)	30 (7.5)	2 (0.6)	2 (0.6)	26 (9.8)	10 (3.9)	78 (19.5)	39 (9.8)	397 (9.8)
AEs leading to discontinuation of D/Pbo	26 (6.5)	15 (3.8)	2 (0.6)	2 (0.6)	26 (9.8)	10 (3.9)	51 (12.7)	25 (6.3)	397 (9.8)
AEs leading to discontinuation of any CTx	48 (12.0)	30 (7.5)	NA	NA	NA	NA	48 (12.0)	30 (7.5)	NA
AEs leading to discontinuation of both D/Pbo and any CTx	20 (5.0)	15 (3.8)	NA	NA	NA	NA	20 (5.0)	15 (3.8)	NA
AEs Leading to on-study surgery not done	7 (1.7)	4 (1.0)	NA	NA	NA	NA	7 (1.7)	4 (1.0)	NA
Any-Grade AEs possibly related to any study treatment	**330 (82.3)**	**313 (78.6)**	**86 (26.5)**	**38 (11.7)**	**131 (49.2)**	**76 (29.9)**	**350 (87.3)**	**325 (81.7)**	**2340 (57.8)**
AEs of max. CTCAE Grade 3 or 4 possibly related to any study treatment	118 (29.4)	130 (32.7)	11 (3.4)	3 (0.9)	20 (7.5)	9 (3.5)	134 (33.4)	133 (33.4)	459 (11.3)
AEs with outcome of death possibly related to any study treatment	3 (0.7)	1 (0.3)	4 (1.2)	0	1 (0.4)	1 (0.4)	7 (1.7)	2 (0.5)	27 (0.7)
Any-Grade imAEs #	**33 (8.2)**	**19 (4.8)**	**19 (5.8)**	**2 (0.6)**	**61 (22.9)**	**21 (8.3)**	**102 (25.4)**	**41 (10.3)**	**705 (17.4)**
imAEs of max. CTCAE Grade 3 or 4	**6 (1.5)**	**5 (1.3)**	**6 (1.8)**	**1 (0.3)**	**6 (2.3)**	**4 (1.6)**	**18 (4.5)**	**10 (2.5)**	**175 (4.3)**

† First dose of study treatment (D/Pbo/CTx) until the date of surgery or, for patients without surgery, up to the earliest of: last dose of neoadjuvant treatment (D/Pbo/CTx) + 90 days, first dose of subsequent anti-cancer therapy, or the DCO date; for assessments recorded on the day of surgery, time was used to determine if it was pre- or post-surgery (if time was not available, it was assumed to occur post-surgery).

‡ Date of surgery (inclusive) to the earliest of 90 days post-surgery, first dose of subsequent anti-cancer therapy, or DCO date.

§ Date of first dose of study treatment post-surgery until earliest of: last study treatment post-surgery + 90 days, date of first dose of subsequent anti-cancer therapy, or DCO date.

¶ First dose of study treatment (D/Pbo/CTx) until the earliest of: the last dose of Study treatment or surgery (taking the latest dose of D/Pbo/CTx/date of surgery) + 90 days, date of the first dose of subsequent anti-cancer therapy, or DCO date.

An AE of special interest consistent with an immune-mediated mechanism of action, where there is no clear alternate etiology, and requiring the use of systemic corticosteroids or other immunosuppressants and/or, for specific endocrine events, endocrine therapy. One patient assigned to the Pbo arm erroneously received a single cycle of D (in the adjuvant phase) and was included in the D arm for the safety analyses.

All reported percentages are based on the total number of patients in each column header as the denominator (i.e., patients who received treatment during that period).
DCO: 10 May 2024 (DCO4).
Source: Table 14.3.2.1.1.IA2, Table 14.3.2.1.2.IA2, Table 14.3.2.1.3.IA2, Table 14.3.2.1.4.IA2, Table 14.3.6.2.1.IA2, Table 14.3.6.2.1.1.IA2, Table 14.3.6.2.1.2.IA2, Table 14.3.6.2.1.3.IA2, Table iemt0617.180, Table iemt0673.048, Table iemt0673.049, Table iemt0673.