ASTRO ANNUAL MEETING 2019

Patterns of Disease Progression with Durvalumab in Stage III NSCLC (PACIFIC)

Andreas Rimner, MD

Memorial Sloan Kettering Cancer Center

Disclosures

- Andreas Rimner has received consulting fees and research grants from AstraZeneca
- This study was sponsored by AstraZeneca
- The author affiliated with MSKCC confirms that, in accordance with GPP3, he did not receive any payment from AstraZeneca related to this publication; additionally, MSKCC did not receive any funding from the study sponsor, AstraZeneca, for this study and its resulting publications. The author affiliated with MSKCC is acting in his individual capacity.

Full author list:

D. Raben,[1] A. Rimner,[2] S. Senan,[3] H. Broadhurst,[4] T. Pellas,[5] P.A. Dennis,[5] and C. Faivre-Finn[6]

[1]University of Colorado Cancer Center, Aurora, CO, [2]Memorial Sloan Kettering Cancer Center, New York, NY, [3]Amsterdam University Medical Centers, Cancer Center Amsterdam, Amsterdam, Netherlands, [4]AstraZeneca, Alderly Park, United Kingdom, [5]AstraZeneca, Gaithersburg, MD, [6]The University of Manchester and The Christie NHS Foundation Trust, Manchester, United Kingdom

Background

- In the phase 3 PACIFIC trial, durvalumab significantly prolonged PFS (HR, 0.52; P <0.0001) and OS (HR, 0.68; P = 0.00251) versus placebo in patients with unresectable, Stage III NSCLC who did not progress after concurrent chemoradiotherapy (cCRT)[1,2,3]
- Time to death or distant metastasis (TTDM) was longer with durvalumab versus placebo (28.3 vs. 16.2 months; HR, 0.53), and the frequency of new lesions was 22.5% and 33.8%, respectively[2]
- Durvalumab was associated with manageable safety and did not detrimentally impact patient-reported outcomes compared to placebo[1,2,4]
- Durvalumab has received global approvals,[3,5] and the 'PACIFIC regimen' (durvalumab after cCRT) has become SoC[6]
- Here, we report exploratory analyses to characterize patterns of disease progression, including the sites of first progression, in patients from PACIFIC

HR, hazard ratio; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; SoC, standard of care;

1. Antonia SJ, et al. N Engl J Med 2017;377:1919–29; 2. Antonia SJ, et al. N Engl J Med. 2018;379:2342–505; 3. European Medicines Agency. Durvalumab (Imfinzi). Summary of product characteristics 2018 [Last accessed 25 July 2019]. Available from: https://www.ema.europa.eu/en/documents/product-information/imfizi-epar-product-information_en.pdf;
4. Hui R, et al. 2019; *In Press*; 5. US Food and Drug Safety Administration. IMFINZI (Durvalumab) Label 2018 [Last accessed 25 July 2019]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761069s002lbl.pdf; 6. National Comprehensive Cancer Network. NCCN Guidelines: Non-small Cell Lung Cancer. 2018

Methods

- Disease progression was assessed by blinded independent central review (BICR; RECIST v1.1)
- Scans were re-evaluated for unequivocal new lesions by a new, independent reviewer*
- New lesions identified within the lung parenchyma or chest wall, including the diaphragm, were categorized as intrathoracic
  - Information on 'in-RT-field' versus 'out-of-RT-field' intrathoracic location was not available
- The proportions of patients with progression (or death), region of first progression, location and number of organs with new lesions, and number of new lesions at progression were descriptively summarized
- Time to progression by region was estimated by Kaplan–Meier method with between-treatment HRs calculated by stratified Log rank test

*A new, separate reviewer to the BICR assessment used for the primary analysis of PFS

First Progression by Location (BICR)*

- Durvalumab reduced first progression versus placebo in all regions (45.4% vs. 64.6%, respectively)
- Overall, intrathoracic progression was the most common (80.6% vs. 74.5% of progressors)

	ITT Population		Subpopulation with Progression	
	Durvalumab (N=476)	Placebo (N=237)	Durvalumab (n=216, 45.4% of ITT)	Placebo (n=153, 64.6% of ITT)
Any RECIST progression, n (%)	216 (45.4)	153 (64.6)	216 (100)	153 (100)
Intrathoracic only	174 (36.6)	114 (48.1)	174 (80.6)	114 (74.5)
Extrathoracic only	33 (6.9)	31 (13.1)	33 (15.3)	31 (20.3)
Intrathoracic and extrathoracic simultaneously	9 (1.9)	8 (3.4)	9 (4.2)	8 (5.2)

*With a data cutoff of March 22, 2018, median duration of follow-up was 25.2 months (range 0.2–43.1)

Time to Progression or Death per BICR (ITT)*

- Durvalumab improved the times to intrathoracic progression only, extrathoracic progression only and simultaneous intrathoracic and extrathoracic progression

	Median time (95% CI) months		**HR (95% CI)**
	Durvalumab (N=476)	Placebo (N=237)	
Type of progression (or death)			
Intrathoracic only	25.2 (19.2–NR)	9.2 (5.6–13.6)	0.55 (0.43–0.70)
Extrathoracic only	NR (NR–NR)	NR (29.3–NR)	0.41 (0.27–0.63)
Intrathoracic and extrathoracic simultaneously	NR (NR–NR)	NR (NR–NR)	0.48 (0.28–0.82)

NR, not reached
*With a data cutoff of March 22, 2018, median duration of follow-up was 25.2 months (range 0.2–43.1)

New Extrathoracic Lesions at First Progression (BICR)*

- Durvalumab reduced new extrathoracic lesions at first progression versus placebo (8.8% vs. 16.5%, respectively)
- Approximately 2/3 of patients had 1 or 2 extrathoracic lesions at first progression

	ITT Population		Subpopulation with Progression and New Extrathoracic Lesions	
	Durvalumab (N=476)	Placebo (N=237)	Durvalumab (n=42, 8.8% of ITT)	Placebo (n=39, 16.5% of ITT)
Any new extrathoracic lesion, n (%)	42 (8.8)	39 (16.5)	42 (100)	39 (100)
1 lesion	19 (4.0)	15 (6.3)	19 (45.2)	15 (38.5)
2 lesions	9 (1.9)	13 (5.5)	9 (21.4)	13 (33.3)
3–5 lesions	9 (1.9)	8 (3.4)	9 (21.4)	8 (20.5)
>5 lesions	5 (1.1)	3 (1.3)	5 (11.9)	3 (7.7)

*With a data cutoff of March 22, 2018, median duration of follow-up was 25.2 months (range 0.2–43.1)

New Extrathoracic Lesions at First Progression by Site (BICR)*

- Most new extrathoracic lesions occurred in a single organ, most commonly in the brain
- The distribution of extrathoracic lesions across organs was similar regardless of treatment

	Subpopulation with Progression and New Extrathoracic Lesions	
	Durvalumab (n=42, 8.8% of ITT)	Placebo (n=39, 16.5% of ITT)
No. of organ locations, n (%)		
1	40 (95.2)	37 (94.9)
2	2 (4.8)	2 (5.1)
Organ location, n (%)		
Brain	26 (61.9)	26 (66.7)
Bone	6 (14.3)	3 (7.7)
Liver	6 (14.3)	5 (12.8)
Lymph nodes	3 (7.1)	3 (7.7)
Other (adrenal gland, myelum, spleen)	3 (7.1)	4 (10.3)

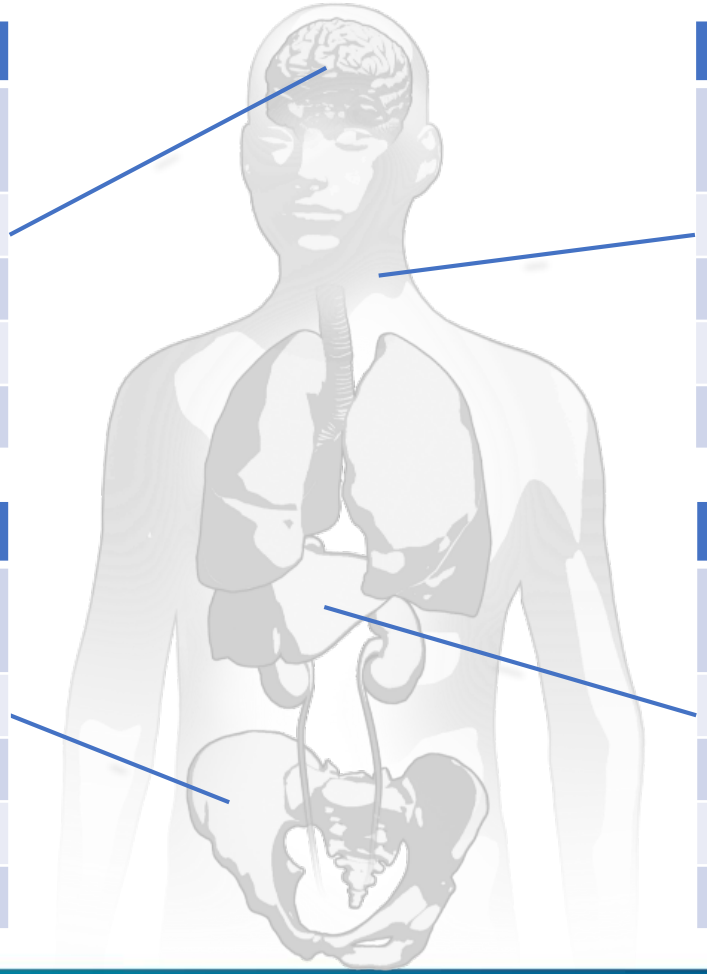
*With a data cutoff of March 22, 2018, median duration of follow-up was 25.2 months (range 0.2–43.1)

New Extrathoracic Lesions at First Progression per Site (BICR)*

- The patterns of extrathoracic lesion numbers per organ were similar regardless of treatment

BRAIN	No. of patients (%)	
No. of new brain lesions	Durvalumab (n=26)	Placebo (n=26)
1	12 (46.2)	9 (34.6)
2	8 (30.8)	9 (34.6)
3–5	6 (23.1)	5 (19.2)
>5	0	3 (11.5)

BONE	No. of patients (%)	
No. of new bone lesions	Durvalumab (n=6)	Placebo (n=3)
1	6 (100)	2 (66.7)
2	0	0
3–5	0	1 (33.3)
>5	0	0



LYMPH NODES	No. of patients (%)	
No. of new lymph node lesions	Durvalumab (n=3)	Placebo (n=3)
1	1 (33.3)	1 (33.3)
2	1 (33.3)	1 (33.3)
3–5	0	1 (33.3)
>5	1 (33.3)	0

LIVER	No. of patients (%)	
No. of new liver lesions	Durvalumab (n=6)	Placebo (n=5)
1	0	3 (60.0)
2	0	2 (40.0)
3–5	2 (33.3)	0
>5	4 (66.7)	0

*With a data cutoff of March 22, 2018, median duration of follow-up was 25.2 months (range 0.2–43.1)

Conclusions

- The addition of durvalumab after cCRT (PACIFIC regimen) reduced rates of progression versus placebo at both intrathoracic and extrathoracic sites
- Durvalumab improved the time to progression versus placebo, regardless of location
  - Most patients experienced an intrathoracic recurrence at first progression, regardless of treatment
- The extrathoracic recurrence patterns at first progression were similar with both treatments
- Most patients who progressed had 1 or 2 extrathoracic lesions, making them potentially amenable to local ablative therapies