BERLIN 2025 ESMO congress

1633P

Onset and progression of atherosclerosis in patients with melanoma treated with immune checkpoint inhibitors

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Background

Immune checkpoint inhibitors (ICIs) are effective anti-cancer agents but significantly increase cardiovascular risk. This could be due to its potential to induce or worsen atherosclerosis. We evaluated the onset and progression of atherosclerosis during ICI treatment in patients with melanoma in five segments of the arterial tree and investigated risk factors for substantial (>10%/year) atherosclerotic plaque growth in the descending thoracic aorta.

Methods

Onset and yearly progression of atherosclerosis were assessed in the aortic arch, descending thoracic aorta, abdominal aorta, left and right iliac arteries via CT scans performed prior to and one year (+/-three months) after ICI therapy initiation in patients with melanoma in the adjuvant and advanced disease setting. The primary outcome was the yearly progression of maximal plaque thickness in each arterial segment. Secondary outcomes were changes in the number of plaques, incidence of arterial thrombosis (ATE), and factors associated with substantial plaque growth in the descending thoracic aorta.

Results

In total, 244 patients were included. Plaque thickness increased significantly in all aortic segments, ranging from +3.0-8.0% per year (Table; all $P<0.001$). In 75% of included patients, substantial plaque growth in ≥1 segment occurred. Number of plaques remained identical in 64-86% of arterial segments. Three patients (1.2%) developed ATE within 1 year after ICI initiation. ICI combination therapy demonstrated a trend towards increased risk of substantial plaque growth compared to monotherapy (OR 2.10 [0.95-4.66; $P=0.068$]), whereas antihypertensive drug usage associated with a lower risk (OR 0.47 [0.26-0.86; $P=0.014$]).Table: 1633P

Segment	Total			Growth ≥10%		
	N (total)	Median growth (%)	*P*-value	N (% of total)	Median growth (%)	*P*-value
Aortic arch	165	8.0 (18)	<0.001	72 (44)	19.0 (21)	<0.001
Descending thoracic aorta	191	5.2 (19)	<0.001	74 (39)	20.0 (16)	<0.001
Abdominal aorta	208	3.0 (17)	<0.001	64 (31)	19.0 (13)	<0.001
Left iliac artery	171	6.5 (25)	<0.001	77 (45)	21.7 (17)	<0.001
Right iliac artery	189	5.6 (19)	<0.001	76 (40)	20.6 (24)	<0.001

Conclusions

The majority of melanoma patients experience substantial atherosclerotic plaque growth during ICI therapy. Possible preventive strategies should be investigated to minimize cardiovascular events while maintaining the beneficial effects of ICI therapy.

Legal entity responsible for the study

The authors.

Funding

Has not received any funding.

Disclosure

R.H. Mathijssen: Financial Interests, Institutional, Invited Speaker: Bayer, Novartis; Financial Interests, Institutional, Advisory Board: Servier, NaDeNo Nanoscience; Financial Interests, Institutional, Research Grant, Investigator-initiated research: Astellas, Bayer, Cristal Therapeutics,

Pfizer, Roche, Sanofi, Servier, Boehringer-Ingelheim, Novartis, Nordic Pharma; Financial Interests, Institutional, Coordinating PI: Pamgene; Financial Interests, Institutional, Funding: Echo Pharmaceuticals, Deuter Oncology. All other authors have declared no conflicts of interest.