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Outcomes of patients who progressed while receiving avelumab + axitinib (A + Ax) and received subsequent treatment (Tx) in JAVELIN Renal 101

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SCOPE



 We describe the outcomes of patients with advanced renal cell carcinoma (aRCC) who received first line A + Ax in the phase 3 JAVELIN Renal 101 trial (NCT02684006) and went on to receive subsequent Tx

CONCLUSIONS



- In patients with aRCC who received second-line (2L) therapies following first-line (1L) Tx with A + Ax, single-agent (SA) vascular endothelial growth factor (receptor) (VEGF[R]) inhibitor was the most frequent therapy
 - The overall survival (OS) in patients receiving 2L treatment was longer compared with patients who discontinued A + Ax and did not receive any subsequent Tx
 - Our findings suggest that the use of 2L treatment upon discontinuation of the combination of a checkpoint inhibitor and a VEGFR tyrosine kinase inhibitor (TKI) is likely to provide a benefit, although further studies are warranted to establish the optimal sequence of Tx

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BACKGROUND

- RCC is the most common kidney cancer and constitutes approximately 3% of all malignant tumors in adults. RCC is often first detected at an advanced stage, with 25% to 30% of patients with metastatic disease at diagnosis¹
- Avelumab is a human immunoglobulin G1 (IgG1) monoclonal antibody targeting PD-L1 that was approved in combination with axitinib, a VEGFR TKI, for 1L Tx of aRCC^{2,3}
- In the phase 3 JAVELIN Renal 101 trial, A + Ax demonstrated significantly longer progression-free survival compared with sunitinib in patients who received these therapies as 1L Tx for aRCC⁴
- There are limited data on the outcomes of patients receiving 2L systemic therapy following immunotherapies plus TKIs in the 1L

METHODS

- In the JAVELIN Renal 101 trial, treatment-naive patients with aRCC were randomized 1:1 to receive avelumab (10 mg/kg intravenously every 2 weeks) + axitinib (5 mg orally twice daily) or sunitinib (50 mg orally once daily for 4 weeks of a 6-week cycle)
- At the cutoff date for the third interim analysis (April 28, 2020), patients who received 1L A + Ax and received any or no subsequent lines of Tx were assessed
- Patients receiving 2L systemic Tx were assessed and grouped in the following categories:
- SA Tx with VEGF(R) or PD-(L) 1 inhibitors or other
- Combination therapy (COMBO) with VEGF(R) inhibitors + other, or any other COMBO
- We report the OS and the time receiving 2L treatment for these groups using the Kaplan-Meier method

RESULTS

- At the cutoff date for the third interim analysis, 346 of 442 patients (78.3%) in the A + Ax arm discontinued treatment with avelumab, and 338 of 442 (76.5%) discontinued axitinib (**Table 1**)
- At least one 2L anticancer drug therapy was received by 204 of 442 (46.2%) patients following A + Ax Tx (**Table 2**)
- The most common 2L Tx was SA VEGF(R) received by 132 of 204 patients, and cabozantinib was the most frequently used SA VEGF(R)
- 2L SA PD-(L) 1 Tx was given in 19 of 204 patients, with nivolumab being the most frequently used agent
- The median OS in patients receiving 2L SA VEGF(R) or PD-(L) 1 inhibitors was 29.8 months (95% CI, 24.1-42.2) and not evaluable (NE), respectively (**Table 3**), and the median time on Tx was 12.1 months (95% CI, 8.4-NE) and 8.9 months (95% CI, 2.3-NE), respectively (**Table 4**)

Table 1. Summary of reason for discontinuation of A + Ax

| | Avelumab (N=442) | Axitinib (N=442) |
|---------------------------------------|---------------------|---------------------|
| Discontinued, n (%) | 346 (78.3) | 338 (76.5) |
| Reason for discontinuation, n (%) | | |
| Death | 22 (5.0) | 24 (5.4) |
| Progressive disease | 175 (39.6) | 187 (42.3) |
| Adverse event | 98 (22.2) | 67 (15.2) |
| Physician decision | 8 (1.8) | 6 (1.4) |
| Global deterioration of health status | 15 (3.4) | 20 (4.5) |
| Withdrawal of patient | 15 (3.4) | 19 (4.3) |
| Study related* | 8 (1.8) | 9 (2.0) |
| Other | 5 (1.1) | 6 (1.4) |
| Ongoing n, (%) | 96 (21.7) | 104 (23.5) |

A, avelumab; Ax, axitinib. *Includes non-compliance with study drug, protocol deviation, and no longer meets eligibility criteria.

Table 2. Summary of follow-up anticancer therapies

| Discontinued, n (%) | Avelumab + axitinib (N=442) | Sunitinib (N=444) |
|---|--------------------------------|----------------------|
| Patients who received ≥1 follow-up anticancer drug therapy, n (%) | | |
| Yes | 204 (46.2) | 269 (60.6) |
| No | 63 (14.3) | 60 (13.5) |
| Not reported | 175 (39.6) | 115 (25.9) |
| Follow-up anticancer drug therapy regimens, n (%) | | |
| 0 regimens | 63 (14.3) | 60 (13.5) |
| 1 regimen | 135 (30.5) | 161 (36.3) |
| 2 regimens | 46 (10.4) | 62 (14.0) |
| 3 regimens | 13 (2.9) | 31 (7.0) |
| ≥4 regimens | 10 (2.3) | 15 (3.4) |
| Not reported | 175 (39.6) | 115 (25.9) |
| Patients who received ≥1 follow-up anticancer radiotherapy, n (%) | | |
| Yes | 80 (18.1) | 76 (17.1) |
| No | 173 (39.1) | 224 (50.5) |
| Not reported | 189 (42.8) | 144 (32.4) |
| Patients who received ≥1 follow-up anticancer surgery, n (%) | | |
| Yes | 29 (6.6) | 32 (7.2) |
| No | 216 (48.9) | 262 (59.0) |
| Not reported | 197 (44.6) | 150 (33.8) |

- 20 of 204 patients received 2L COMBO with VEGF(R) + other, with the combination of lenvatinib + everolimus being more frequently used, while 21 of 204 patients received any other COMBO
- The median OS in patients receiving 2L COMBO VEGF(R) + other or any other COMBO was not reached in either arm (Table 3), and the median time on treatment was 12.9 months (95% CI, 8.3-NE) and 11.1 months (95% CI, 3.0-NE), respectively (**Table 4**)
- 124 patients discontinued A + Ax without receiving subsequent anticancer drug therapies. The median OS in this group was 21.3 months (95% CI, 13.3-29.7) (**Table 5**)

Table 3. Summary of OS in patients who received subsequent treatment

| | Single agent (N=163 | 8)* | Combination therap | y (N=41) | | | | |
|--|---------------------|---------------------|----------------------------|------------------------------|--|--|--|--|
| | VEGF(R) (n=132) | PD-(L)1 (n=19) | VEGF(R) + others (n=20) | Any other combination (n=21) | | | | |
| Patients with event, n (%) | 73 (55.3) | 8 (42.1) | 8 (40.0) | 6 (28.6) | | | | |
| Patients censored, n (%) | 59 (44.7) | 11 (57.9) | 12 (60.0) | 15 (71.4) | | | | |
| Probability of being event free (95% CI) | | | | | | | | |
| At 12 months | 0.854 (0.781-0.904) | 0.895 (0.641-0.973) | 1.000 (1.000-1.000) | 0.905 (0.670-0.975) | | | | |
| At 18 months | 0.739 (0.654-0.806) | 0.895 (0.641-0.973) | 0.850 (0.604-0.949) | 0.854 (0.613-0.951) | | | | |
| At 24 months | 0.592 (0.503-0.671) | 0.684 (0.428-0.844) | 0.750 (0.500-0.887) | 0.754 (0.506-0.890) | | | | |
| At 36 months | 0.416 (0.324-0.505) | 0.568 (0.317-0.757) | 0.551 (0.288-0.751) | 0.700 (0.449-0.853) | | | | |
| OS (95% CI), months | | | | | | | | |
| Q1 | 17.7 (15.1-21.3) | 21.1 (4.2-NE) | 26.4 (14.2-NE) | 27.7 (6.4-NE) | | | | |
| Median | 29.8 (24.1-42.2) | NE (21.1-NE) | NE (23.3-NE) | NE (27.7-NE) | | | | |
| Q3 | NE (42.2-NE) | NE (NE-NE) | NE (NE-NE) | NE (NE-NE) | | | | |

Twelve patients in the single-agent arm did not receive therapy with VEGF(R) or PD-(L)1 inhibitors and were not included in analysis.

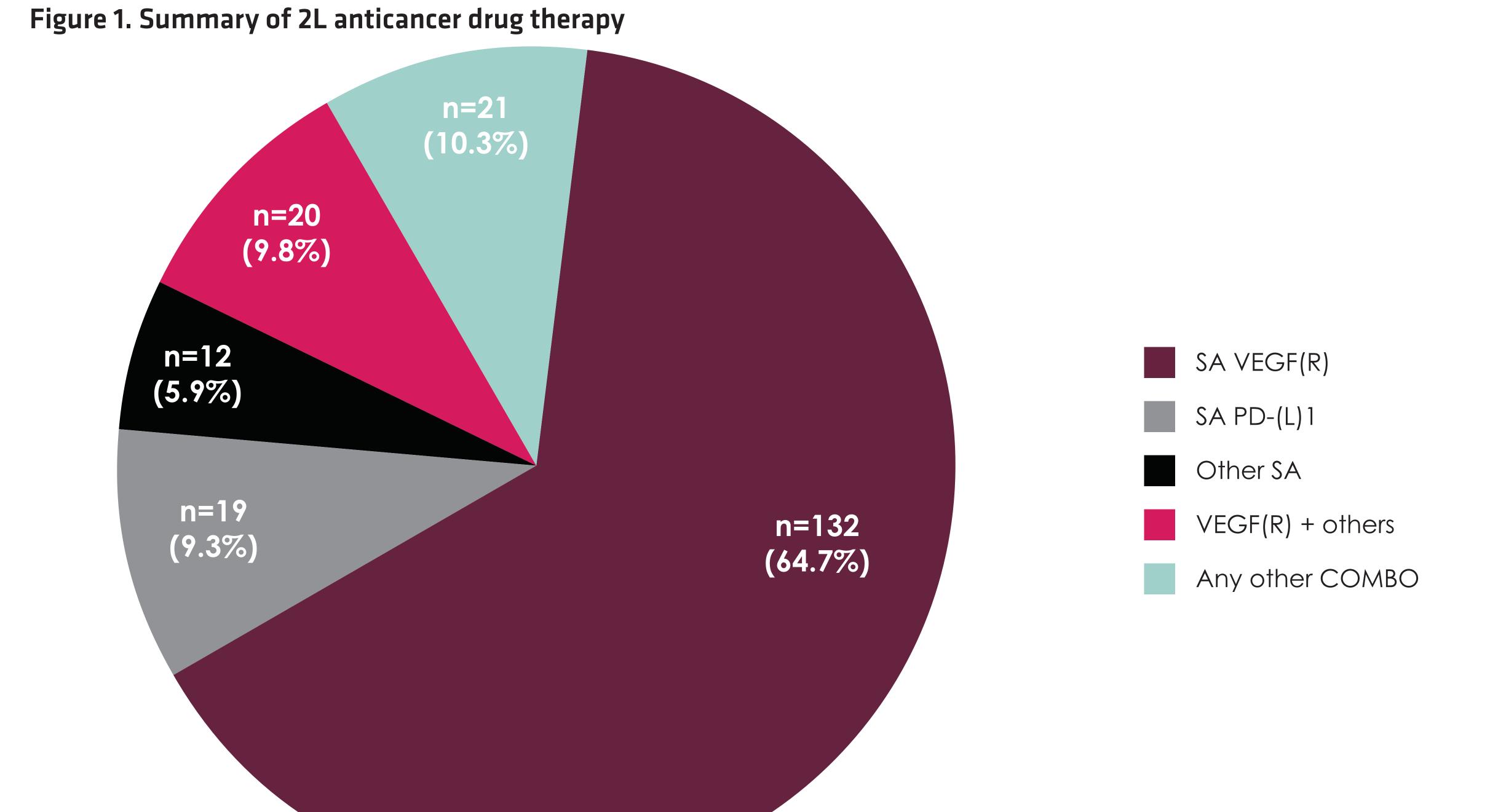
Table 4. Summary of time on 2L treatment

| | Single agent (N=1 | 63) | Combination therapy (N=41) | | | | | | | | |
|---|--------------------|-------------------|----------------------------|------------------------------|--|--|--|--|--|--|--|
| | VEGF(R) (n=132) | PD-(L)1 (n=19) | VEGF(R) + others (n=20) | Any other combination (n=21) | | | | | | | |
| Discontinuation of 2L treatment event, n (%) | 67 (50.8) | 11 (57.9) | 10 (50.0) | 10 (47.6) | | | | | | | |
| Patients censored, n (%) | 65 (49.2) | 8 (42.1) | 10 (50.0) | 11 (52.4) | | | | | | | |
| Median time to discontinuation of 2L treatment (95% CI), months | 12.1 (8.4-NE) | 8.9 (2.3-NE) | 12.9 (8.3-NE) | 11.1 (3.0-NE) | | | | | | | |
| 2L, second line; NE, not evaluable; VEGF(R), vascular endothelial growth factor (receptor). | | | | | | | | | | | |

Table 5. Summary of OS in patients who discontinued A + Ax and did not receive subsequent anticancer drug therapy

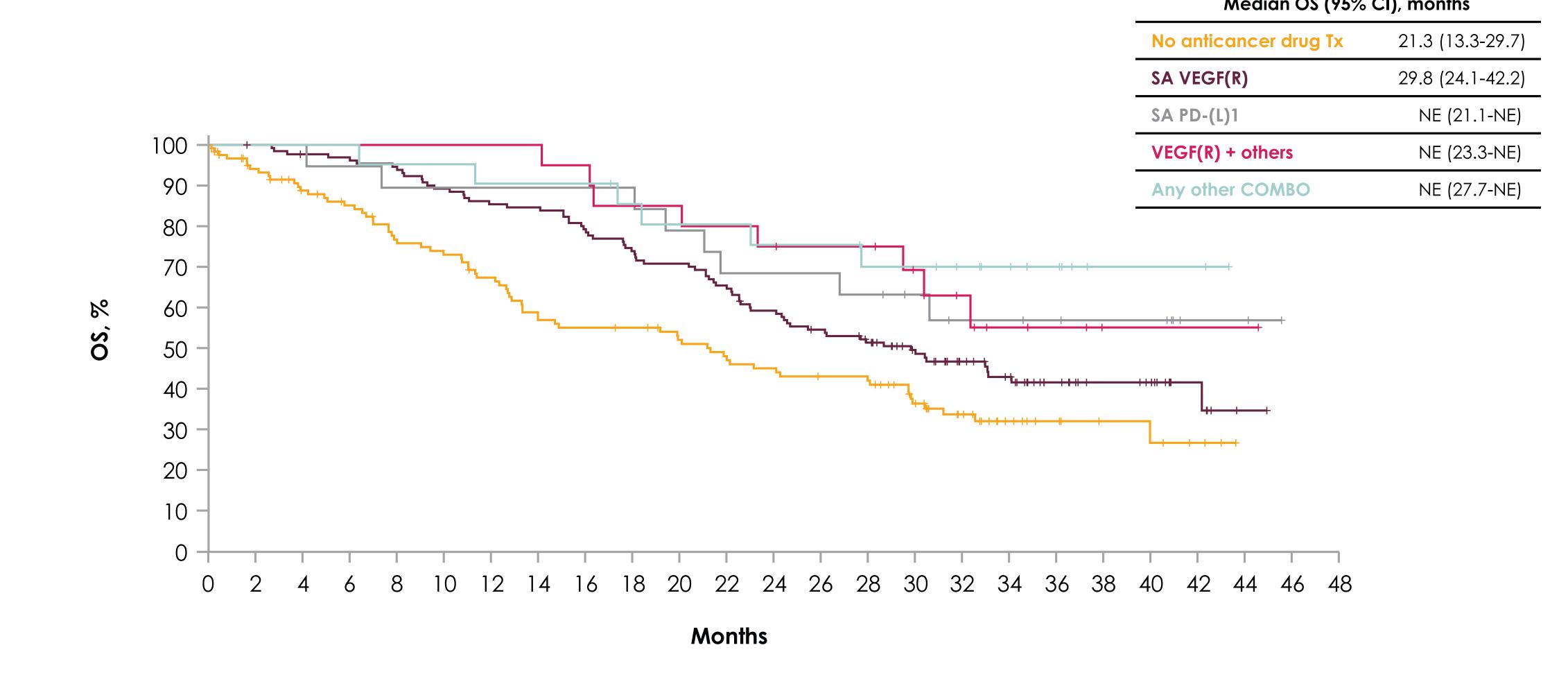
| | No subsequent anticancer drug therapy (N=124) |
|--|---|
| Patients with event, n (%) | 71 (57.3) |
| Patients censored, n (%) | 53 (42.7) |
| Probability of being event free (95% CI) | |
| At 12 months | 0.673 (0.577-0.753) |
| At 18 months | 0.550 (0.451-0.638) |
| At 24 months | 0.450 (0.353-0.542) |
| At 36 months | 0.320 (0.228-0.416) |
| OS (95% CI), months | |
| Q1 | 9.0 (6.7-12.2) |
| Median | 21.3 (13.3-29.7) |
| Q3 | NE (31.2- NE) |

A, avelumab; **Ax**, axitinib; **NE**, not evaluable; **OS**, overall survival.



COMBO, combination therapy; SA, single agent; VEGF(R), vascular endothelial growth factor (receptor).

Figure 2. Summary of OS



No. at risk

| No anticancer drug Tx | 124 | 108 | 98 | 92 | 82 | 78 | 71 | 60 | 58 | 57 | 52 | 48 | 45 | 42 | 41 | 31 | 22 | 13 | 9 | 6 | 5 | 3 | 0 | |
|-----------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|----|----|---|---|---|
| SA VEGF(R) | 132 | 131 | 127 | 126 | 123 | 116 | 111 | 110 | 103 | 96 | 92 | 85 | 76 | 69 | 63 | 52 | 40 | 33 | 22 | 16 | 14 | 6 | 1 | (|
| SA PD-(L)1 | 19 | 19 | 19 | 18 | 17 | 17 | 17 | 17 | 17 | 17 | 15 | 13 | 13 | 13 | 12 | 10 | 8 | 8 | 7 | 6 | 6 | 2 | 2 | (|
| VEGF(R) + others | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 19 | 17 | 17 | 16 | 15 | 14 | 14 | 11 | 8 | 5 | 3 | 1 | 1 | 1 | 1 | (|
| Any other COMBO | 21 | 21 | 21 | 21 | 20 | 20 | 19 | 19 | 19 | 17 | 16 | 16 | 15 | 15 | 13 | 13 | 11 | 9 | 6 | 2 | 2 | 2 | 0 | |

COMBO, combination therapy; NE, not evaluable; SA, single agent; Tx, treatment; VEGF(R), vascular endothelial growth factor (receptor).

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