Differences in Response to Treatment of Advanced Renal Cell Carcinoma With Nivolumab Versus Everolimus in Japanese Individuals

A Subgroup Analysis From the CheckMate 025 Study

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How do the efficacies of nivolumab and everolimus for treatment of advanced renal cell carcinoma differ in the Japanese population?

Background Information

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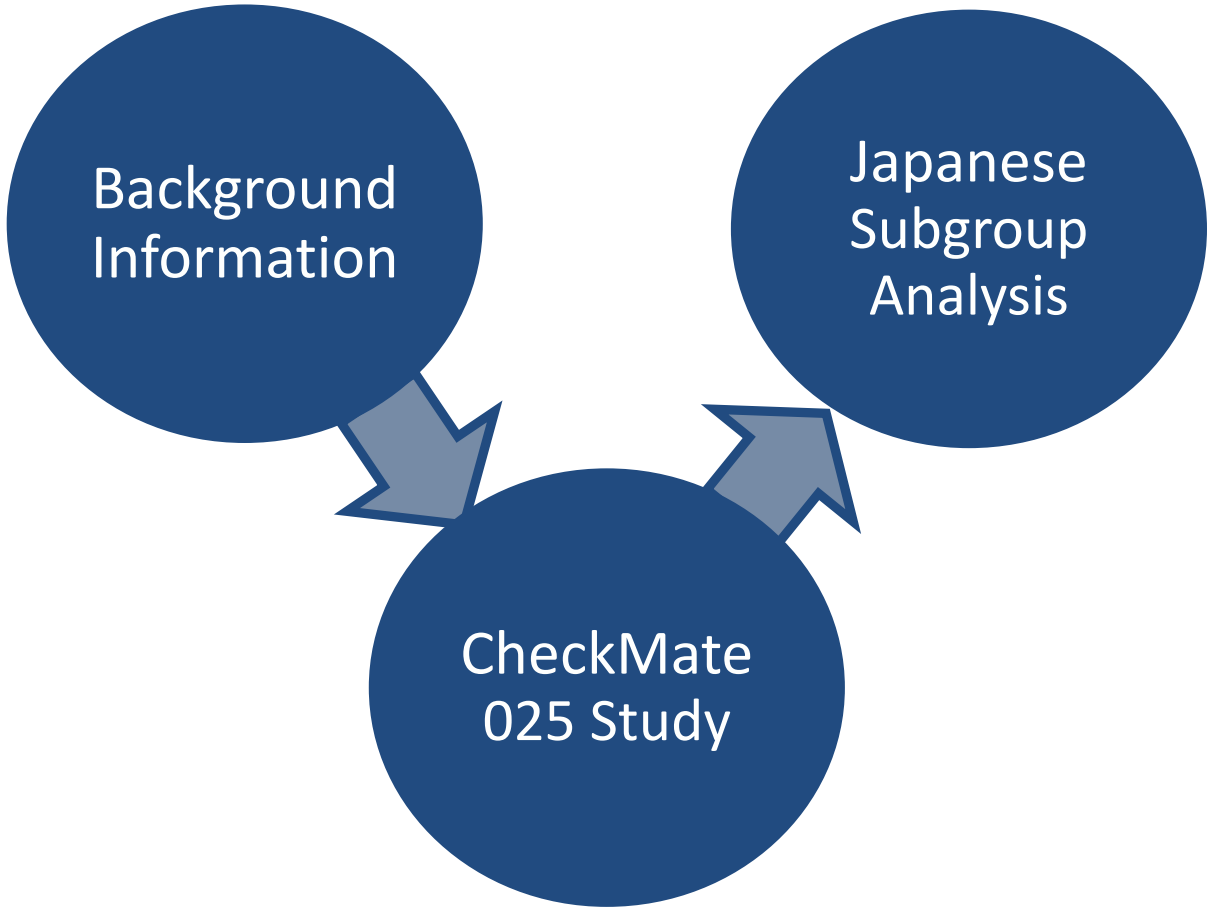

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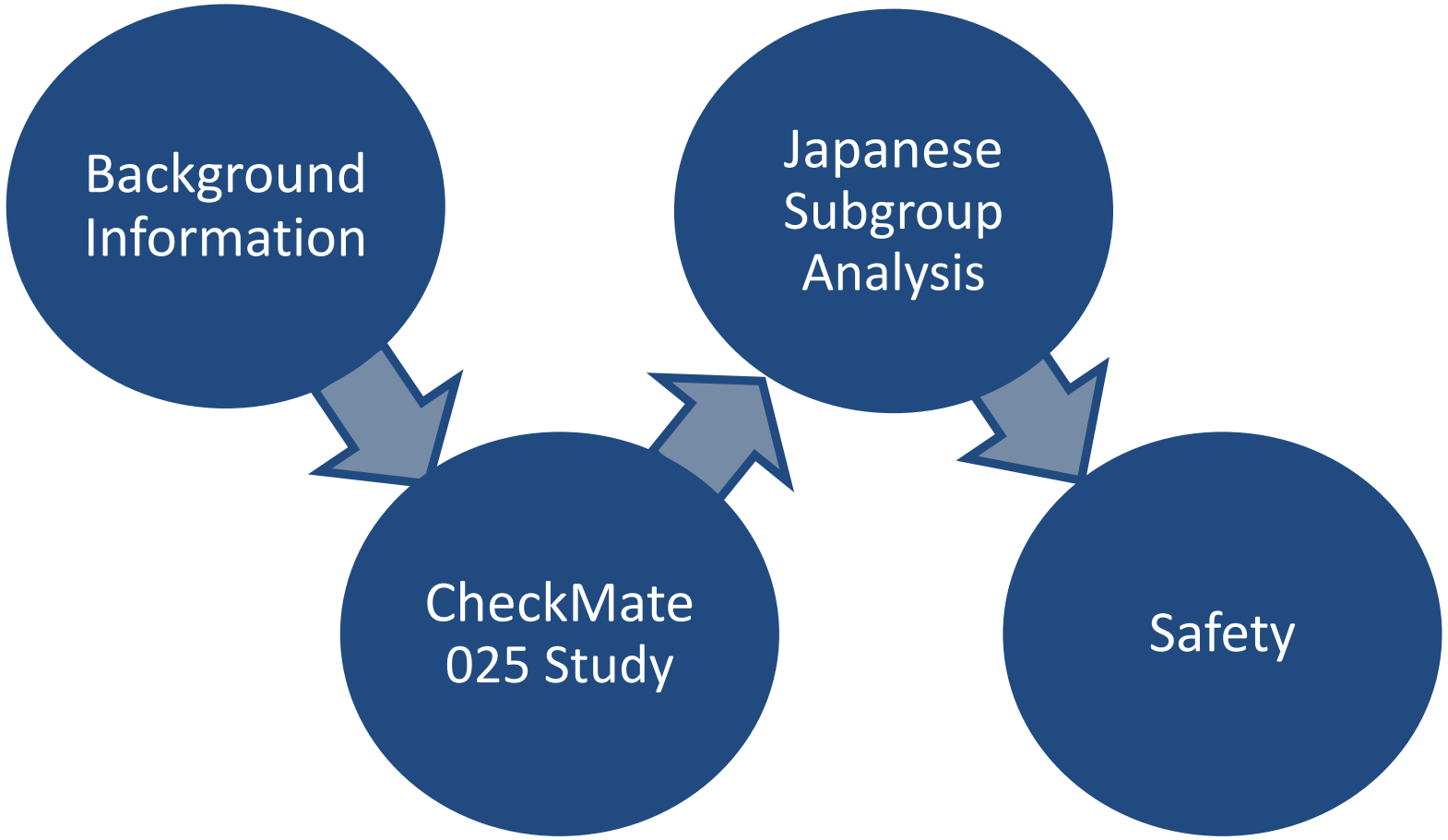

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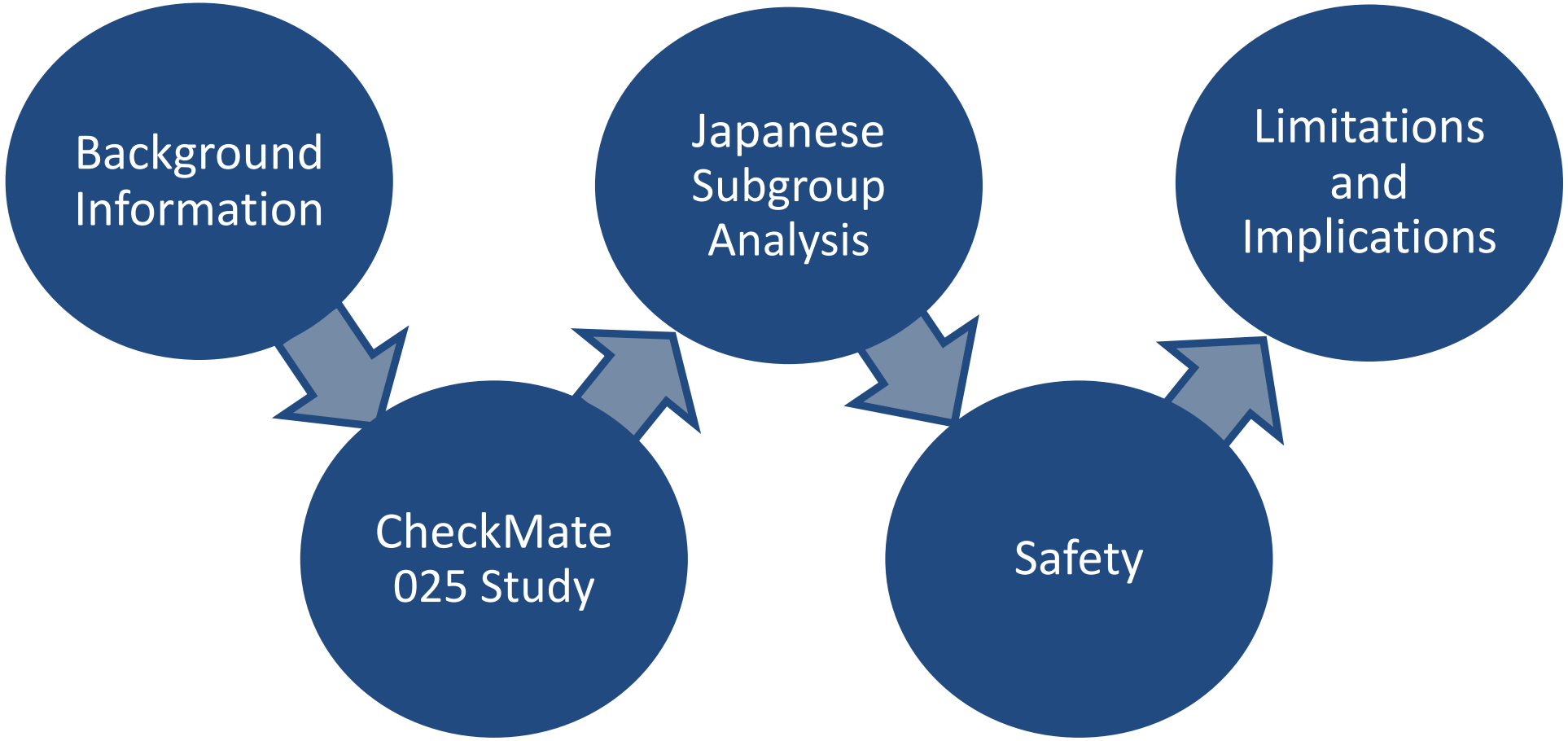


Differences in efficacy and safety of advanced renal cell carcinoma treatment are noted in the Japanese population, an often under-represented population in clinical trials.

1. Tomita Y, Fukasawa S, Shinohara N, et al. Nivolumab versus everolimus in advanced renal cell carcinoma: Japanese subgroup analysis from the CheckMate 025 study. *Jpn J Clin Oncol*. 2017;47(7):639-646. doi:10.1093/jjco/hyx049

Background information

In 2015, there were 6 targeted therapies for advanced renal cell carcinoma approved in Japan

Tyrosine Kinase Inhibitors	Mammalian Target of Rapamycin Inhibitors
Sorafenib	Everolimus
Sunitinib	Temsirolimus
Axitinib	
Pazopanib	

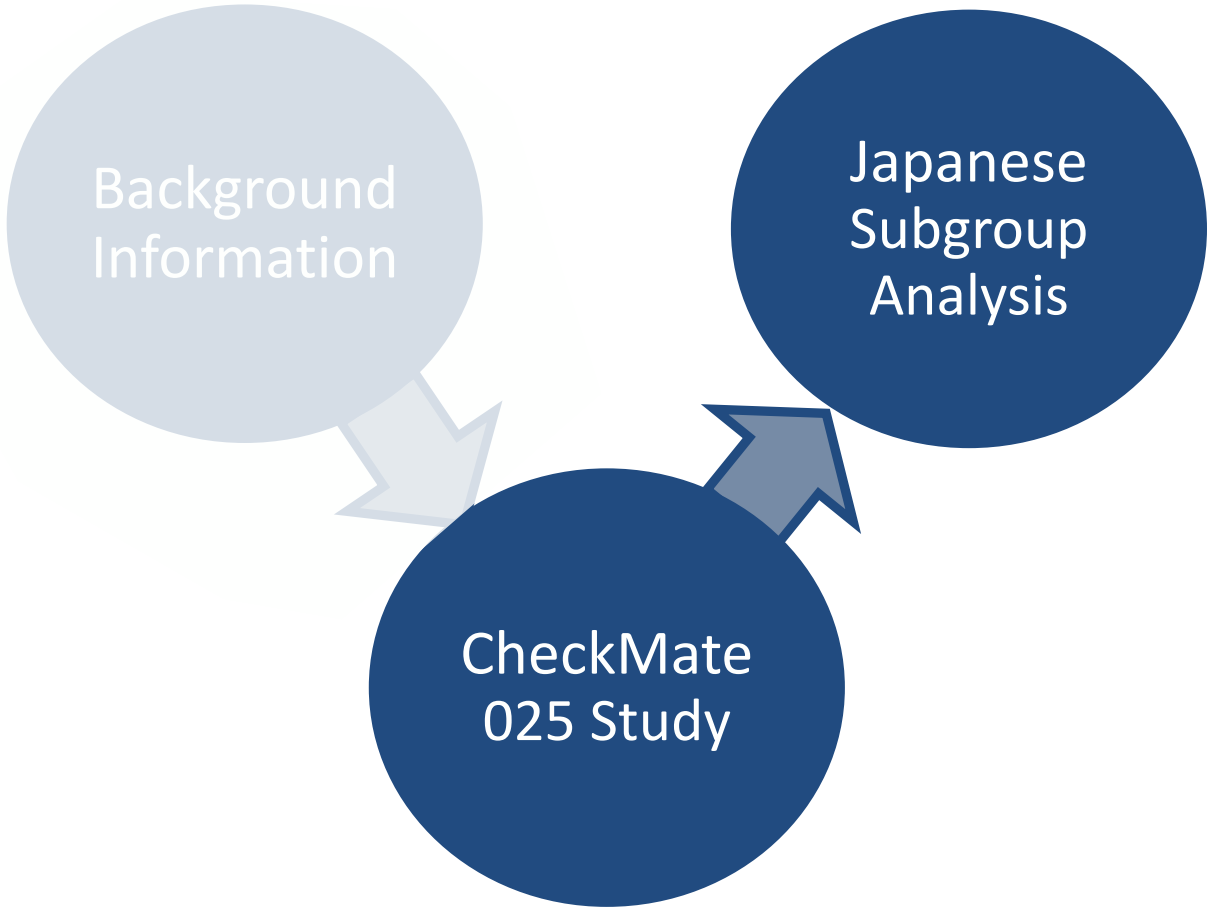
1. Yoshimura K, Uemura H. Pharmacotherapies for renal cell carcinoma in Japan. *Int J Urol*. 2016 Mar;23(3):194-202. doi: 10.1111/iju.13008
2. Motzer RJ, Jonasch E, Agarwal N, et al. Kidney Cancer, Version 2.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2017;15(6):804-834. doi:10.6004/jnccn.2017.0100

The CheckMate 025 study compared nivolumab with everolimus

Tyrosine Kinase Inhibitors	Mammalian Target of Rapamycin Inhibitors	Programmed Death-1 Immune Checkpoint Inhibitor
Sorafenib Sunitinib Axitinib Pazopanib	**Everolimus**	**Nivolumab**

1. Motzer RJ, Escudier B, McDermott DF, et al. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. *N Engl J Med*. 2015;373(19):1803-1813. doi:10.1056/NEJMoa1510665
2. Hamid O, Carvajal RD. Anti-programmed death-1 and anti-programmed death-ligand 1 antibodies in cancer therapy. *Expert Opin Biol Ther*. 2013;13(6):847-861. doi:10.1517/14712598.2013.770836

The CheckMate 025 study compared nivolumab with everolimus in a global population



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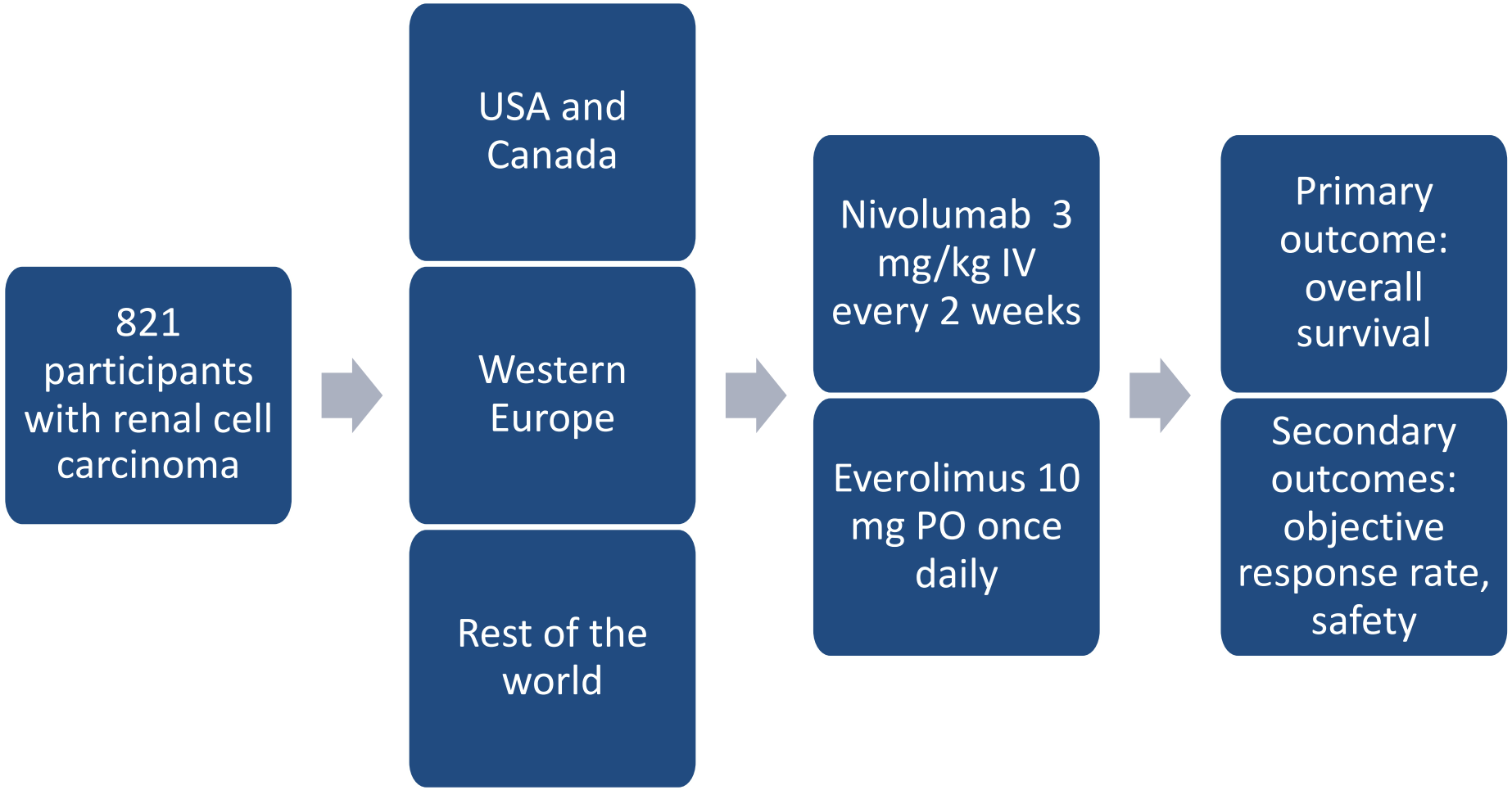

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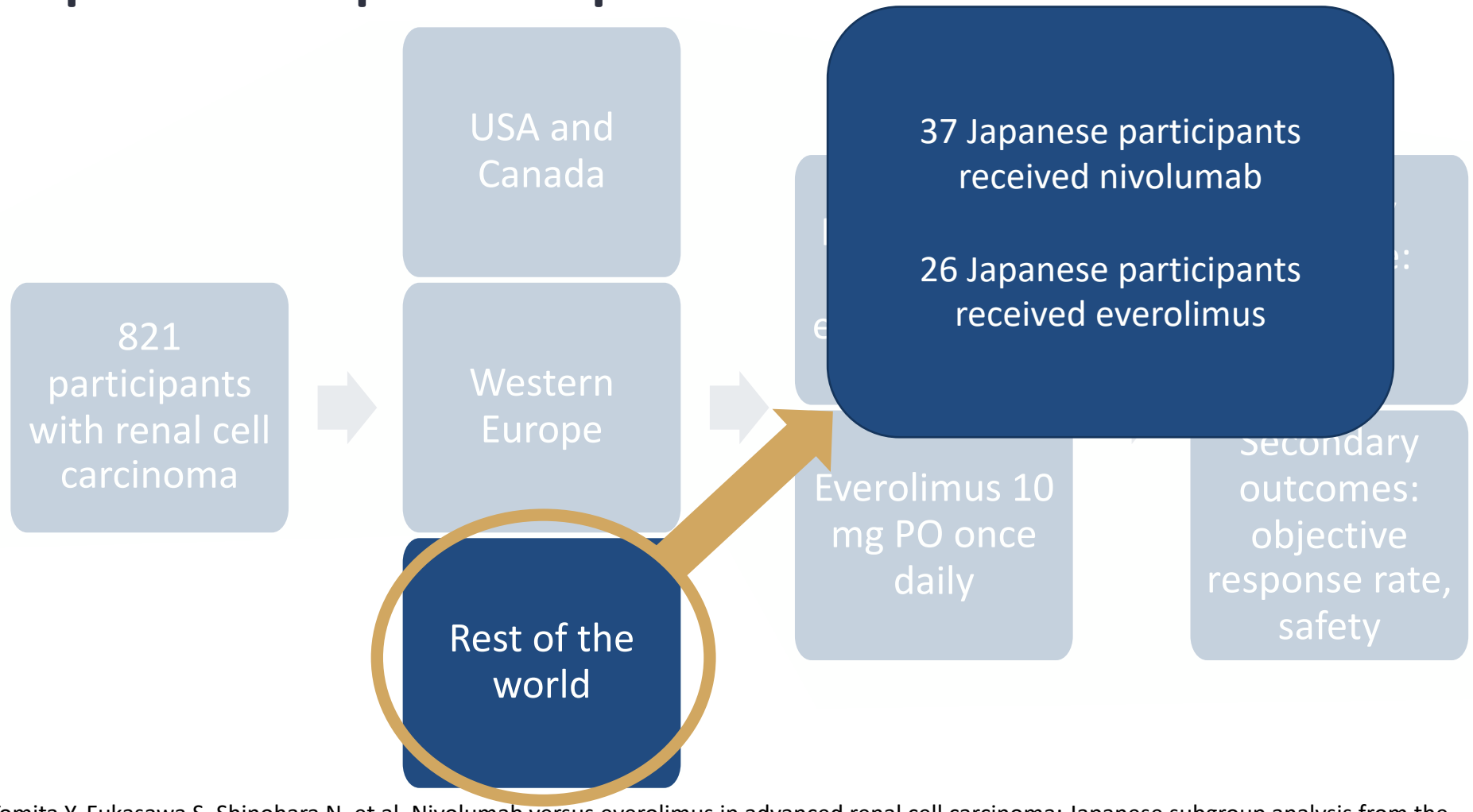
A subgroup analysis was performed in Japanese participants



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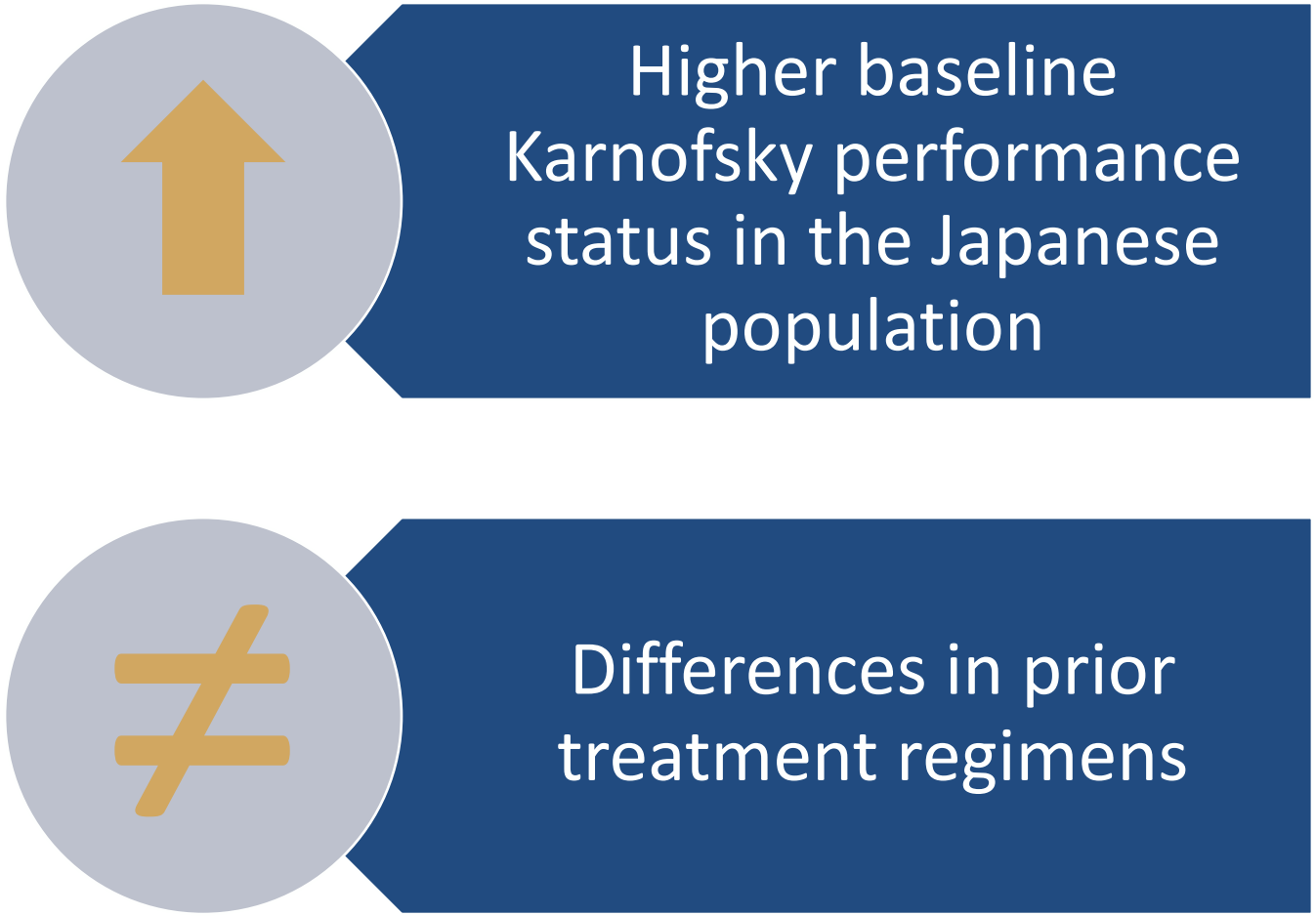
Differences were noted in baseline characteristics of the Japanese subgroup compared with the original study population



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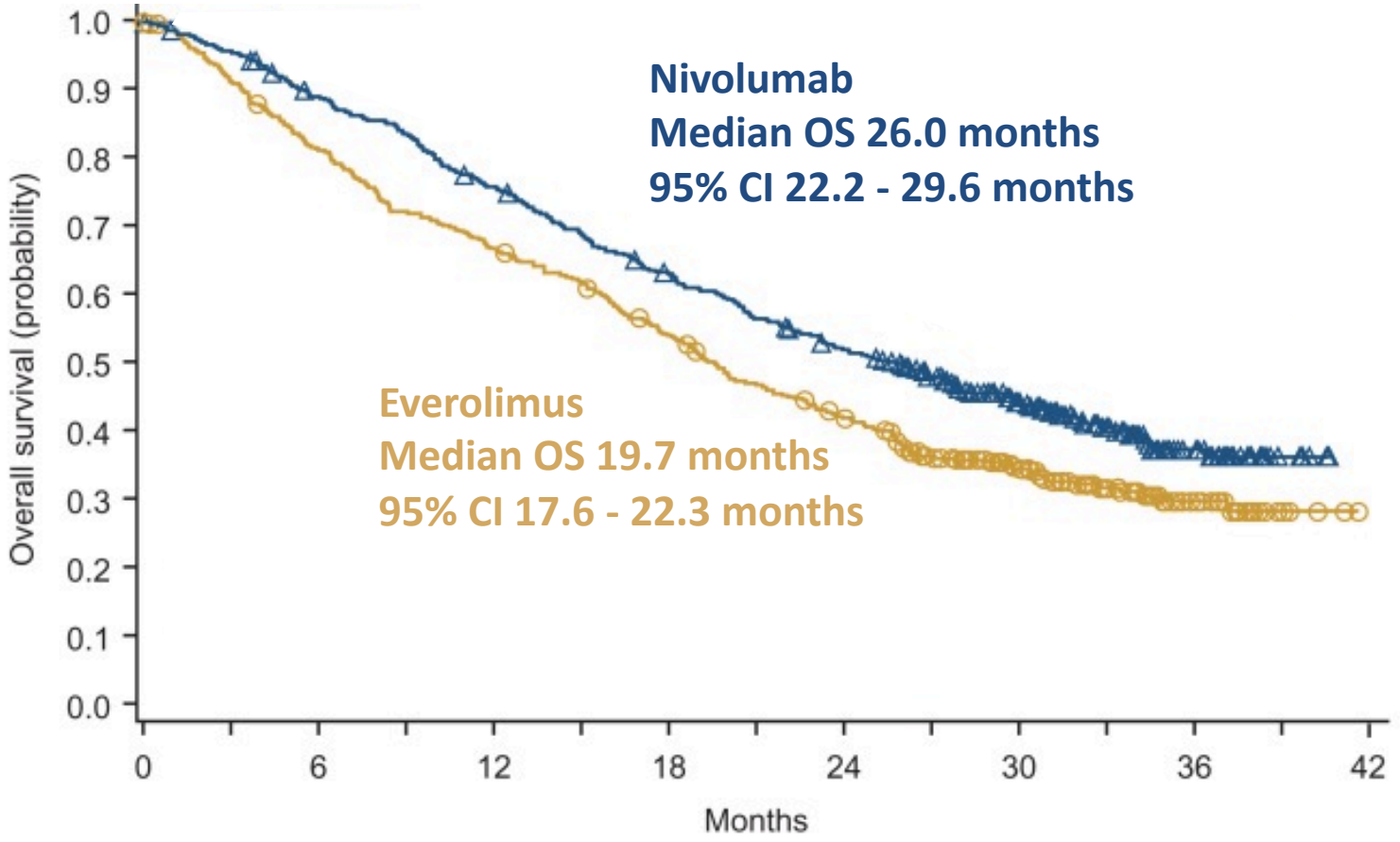
Differences were noted in baseline characteristics of the Japanese nivolumab subgroup compared with the everolimus subgroup

Everolimus Japanese Subgroup

- Sites of metastasis
- Liver metastasis
- Programmed cell death-1 ligand 1 expression

1. Tomita Y, Fukasawa S, Shinohara N, et al. Nivolumab versus everolimus in advanced renal cell carcinoma: Japanese subgroup analysis from the CheckMate 025 study. *Jpn J Clin Oncol*. 2017;47(7):639-646. doi:10.1093/jjco/hyx049

Nivolumab increased overall survival (OS) in the global population



Hazard ratio 0.73
95% CI 0.61 - 0.88
P = .0006

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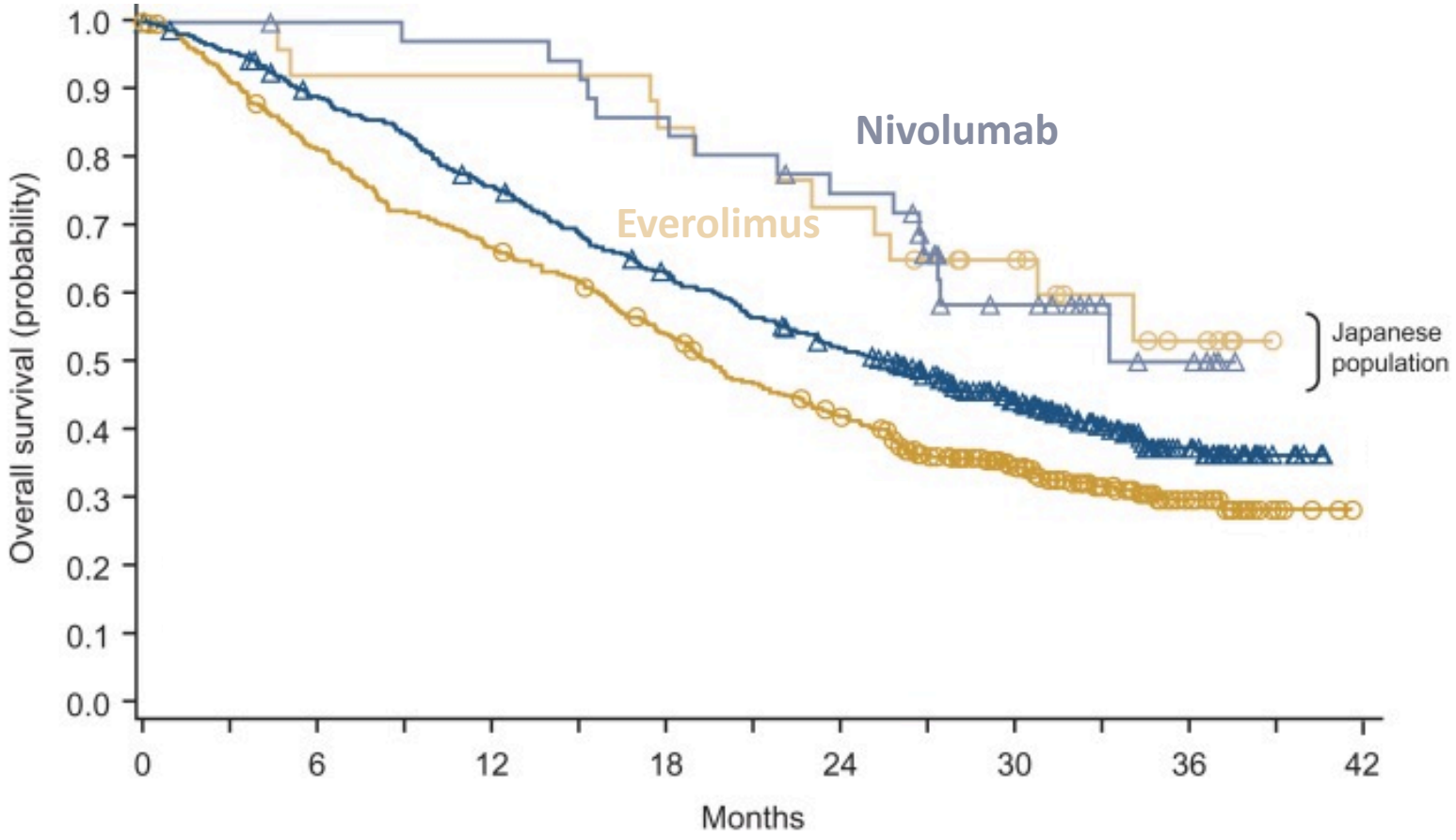
Overall survival was higher in the Japanese subgroup for both nivolumab and everolimus



Hazard ratio 1.05
95% CI 0.48 - 0.2.30

Median OS not reached for either group

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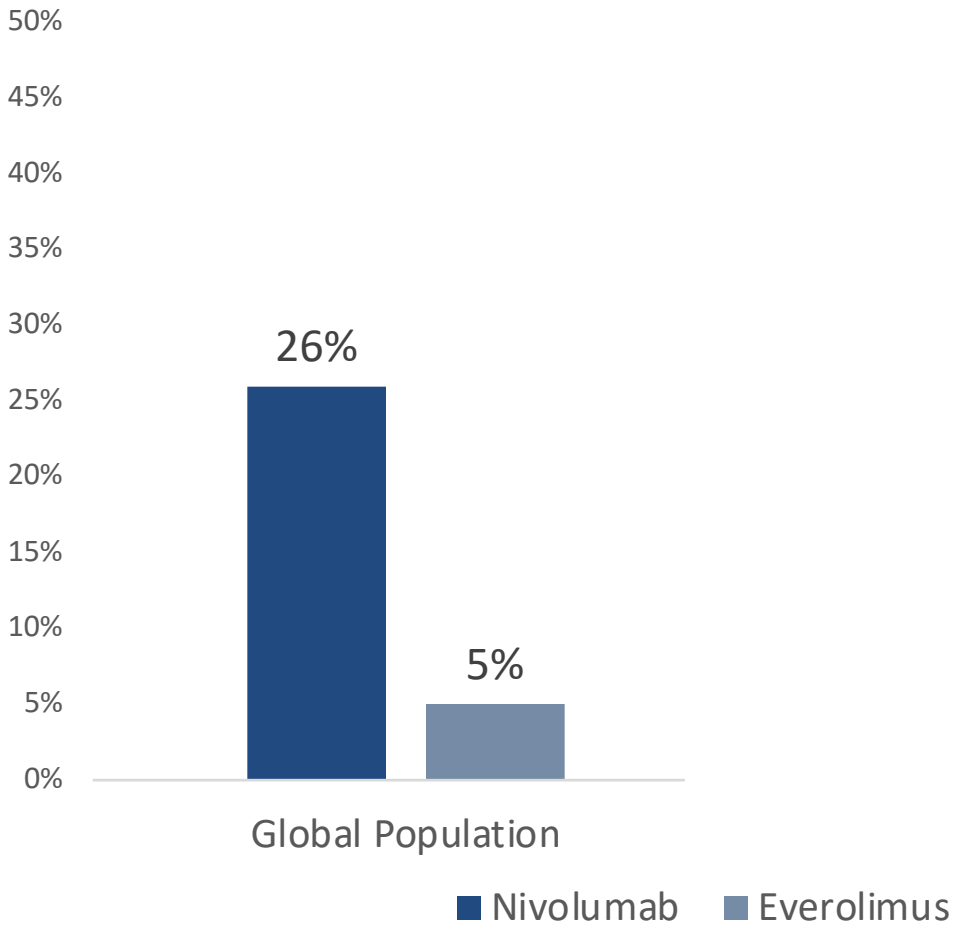
Nivolumab showed an increased objective response rate in the global population



Odds ratio for response 6.13
95% CI 3.77 - 9.95

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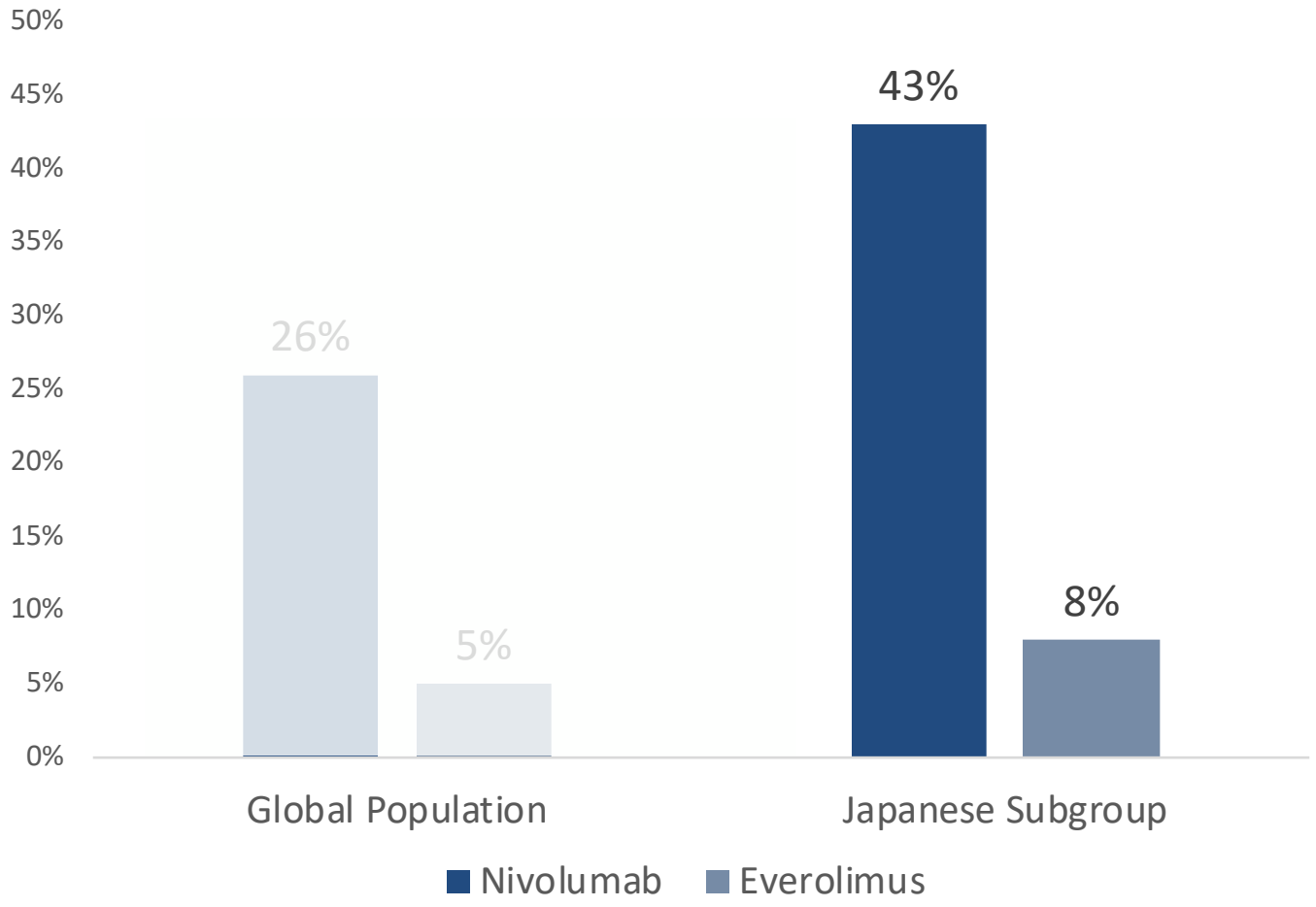
The increase in objective respo nivolumab was more pronounced in the Japanese subgroup



Odds ratio for response rate 9.14
95% CI 1.76 - 88.33

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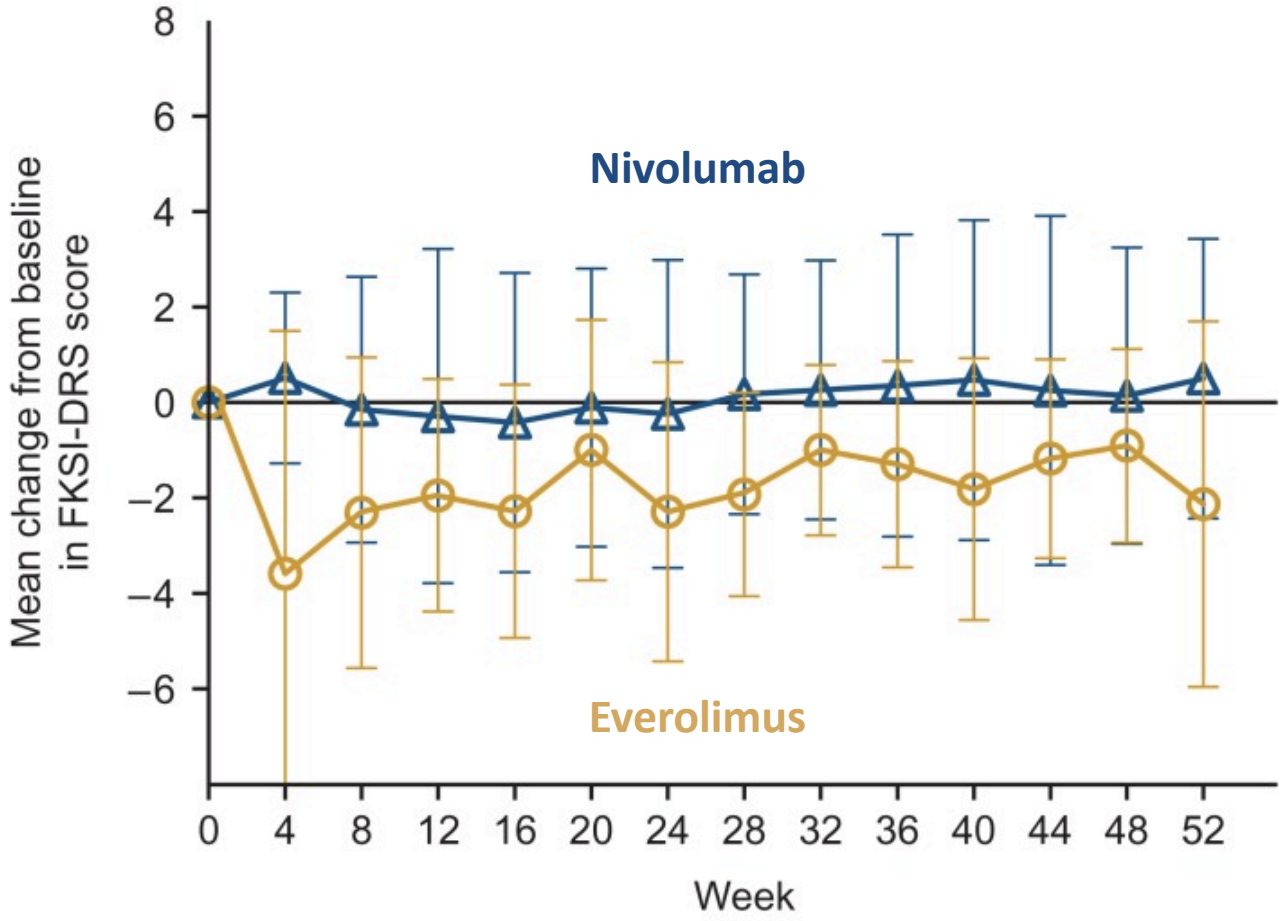
Quality of life was decreased in the everolimus group and stable in the nivolumab group



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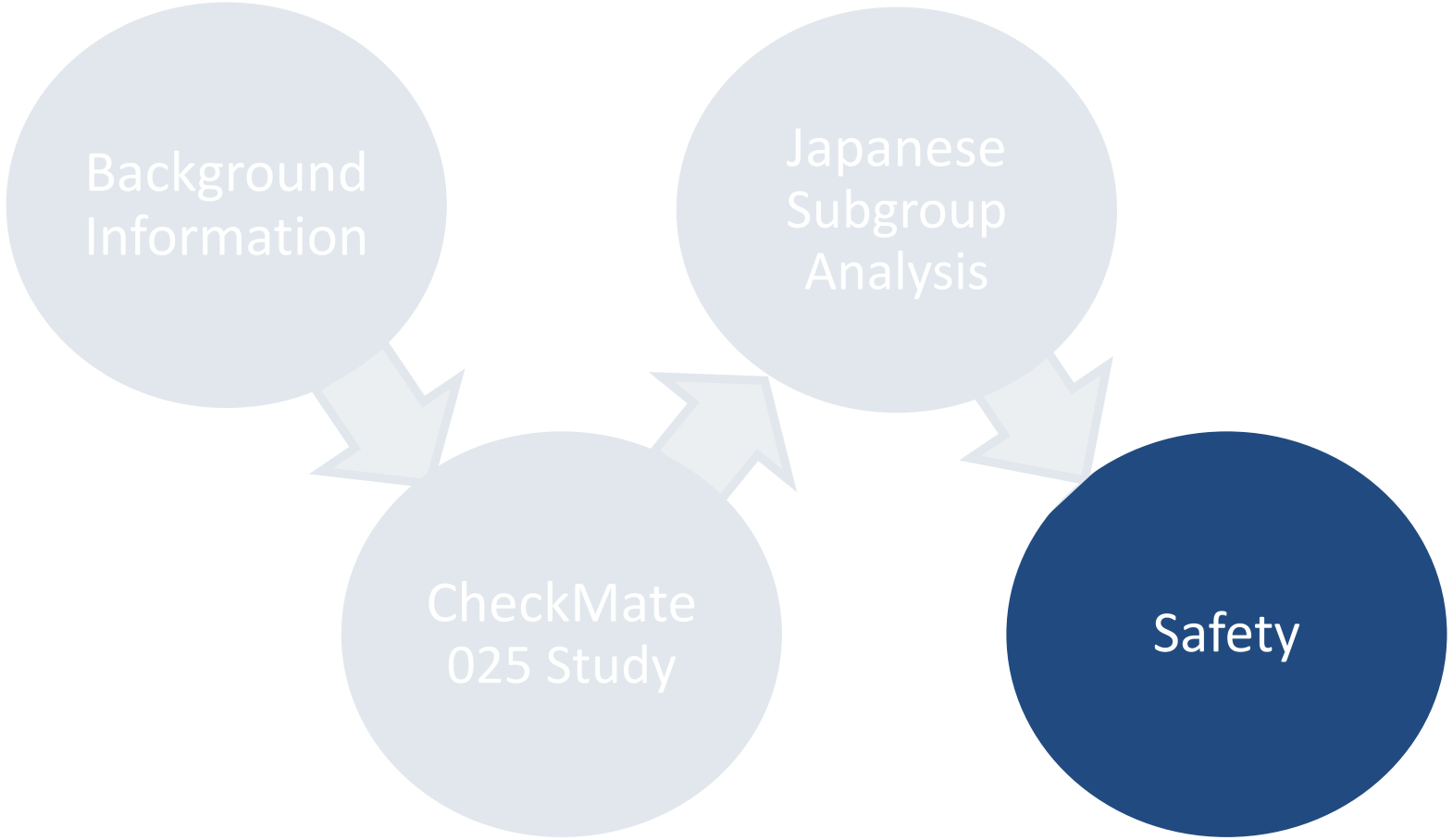
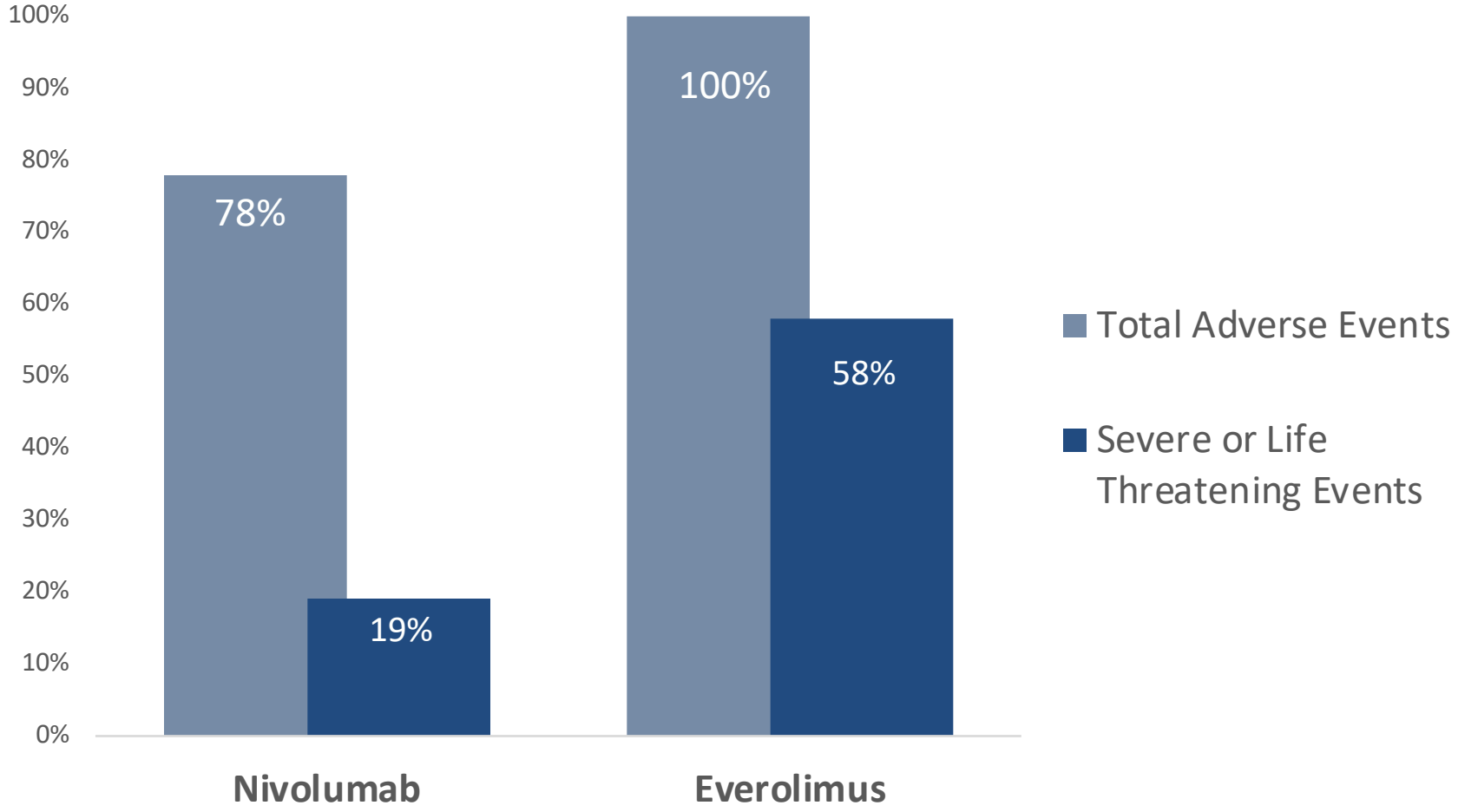
Adverse events



The nivolumab group had a lower rate of adverse events in the Japanese subgroup



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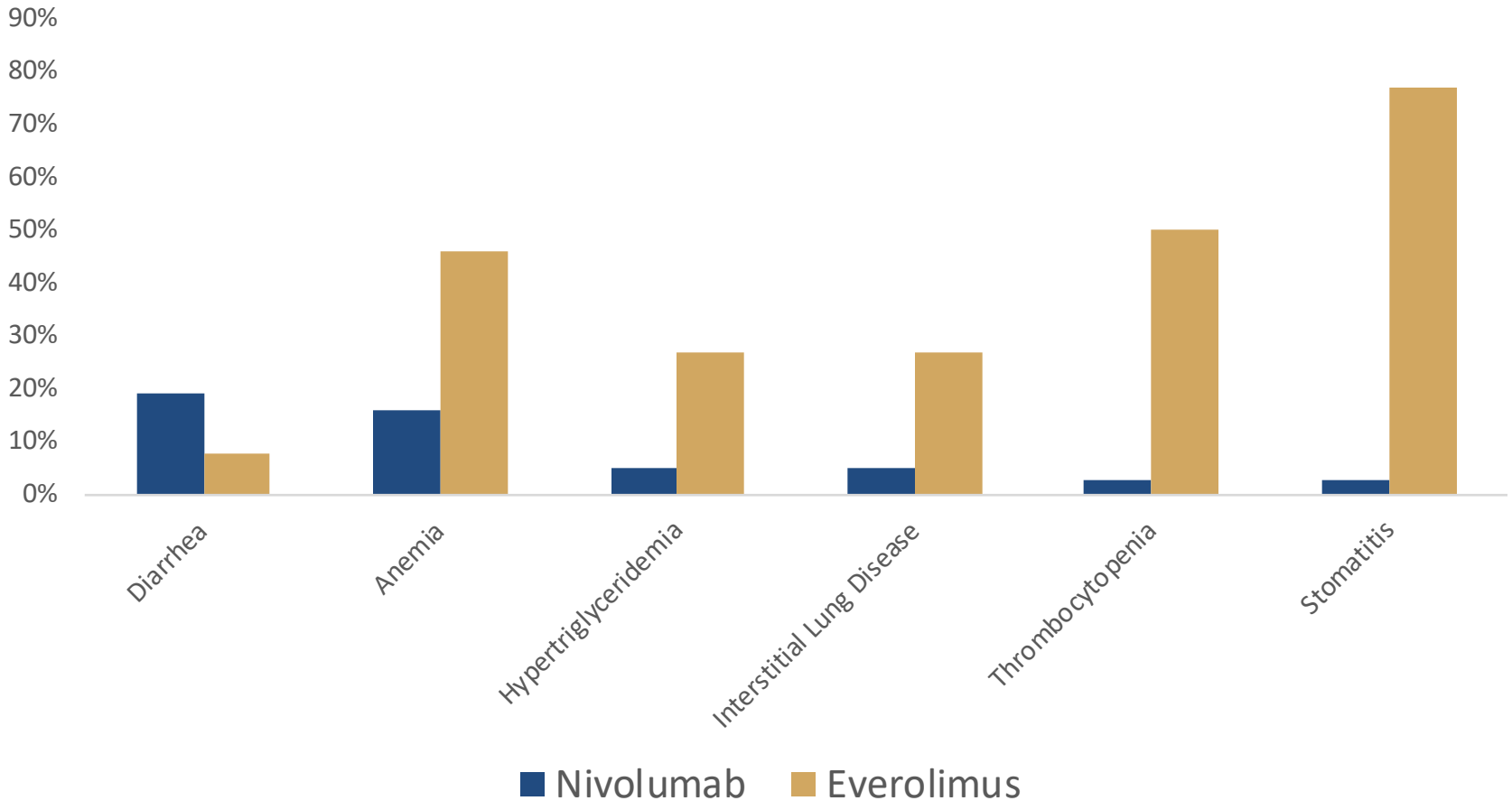
Adverse events in the Japanese population



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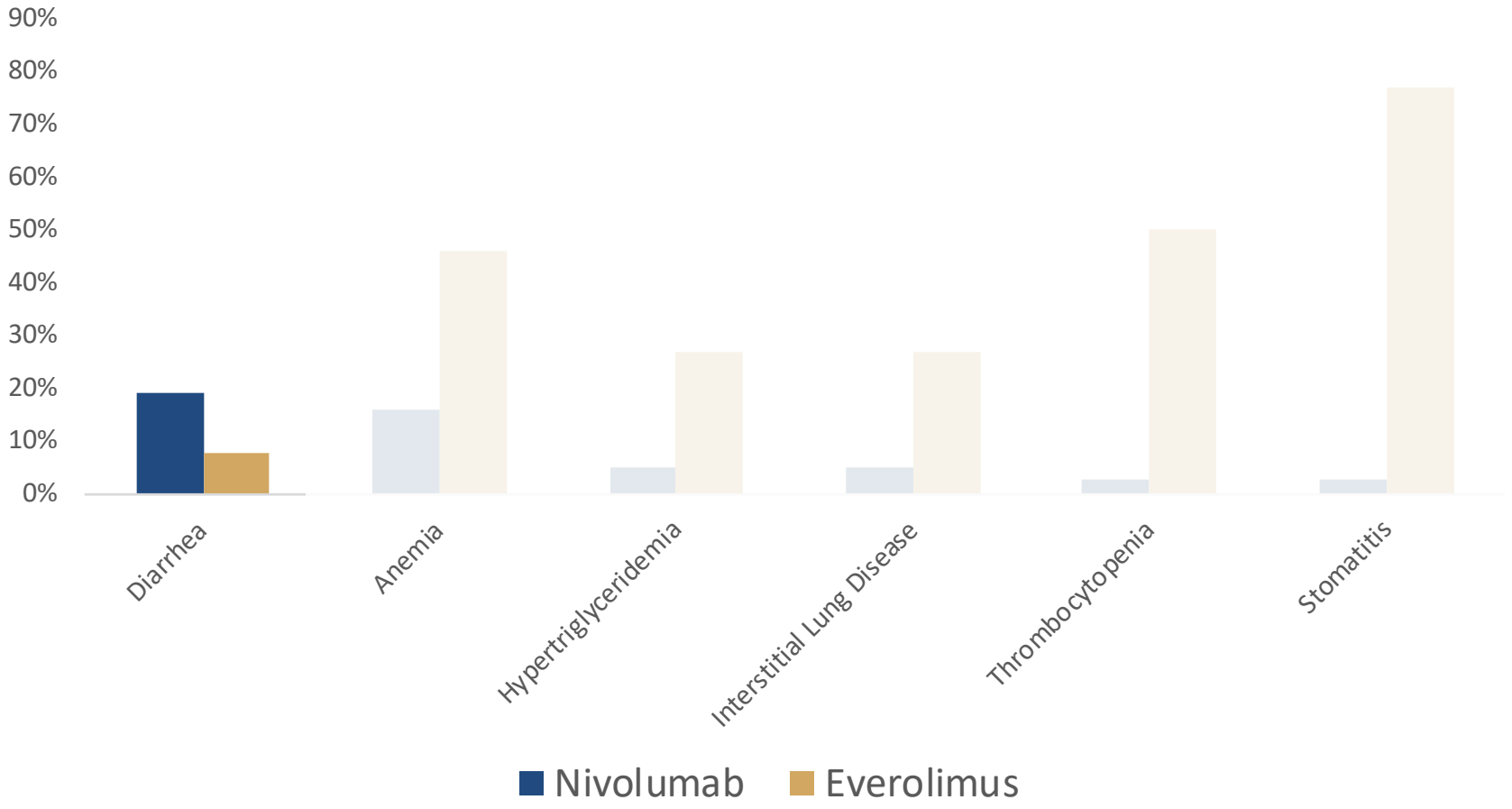
Diarrhea was more common in the nivolumab group of the Japanese population



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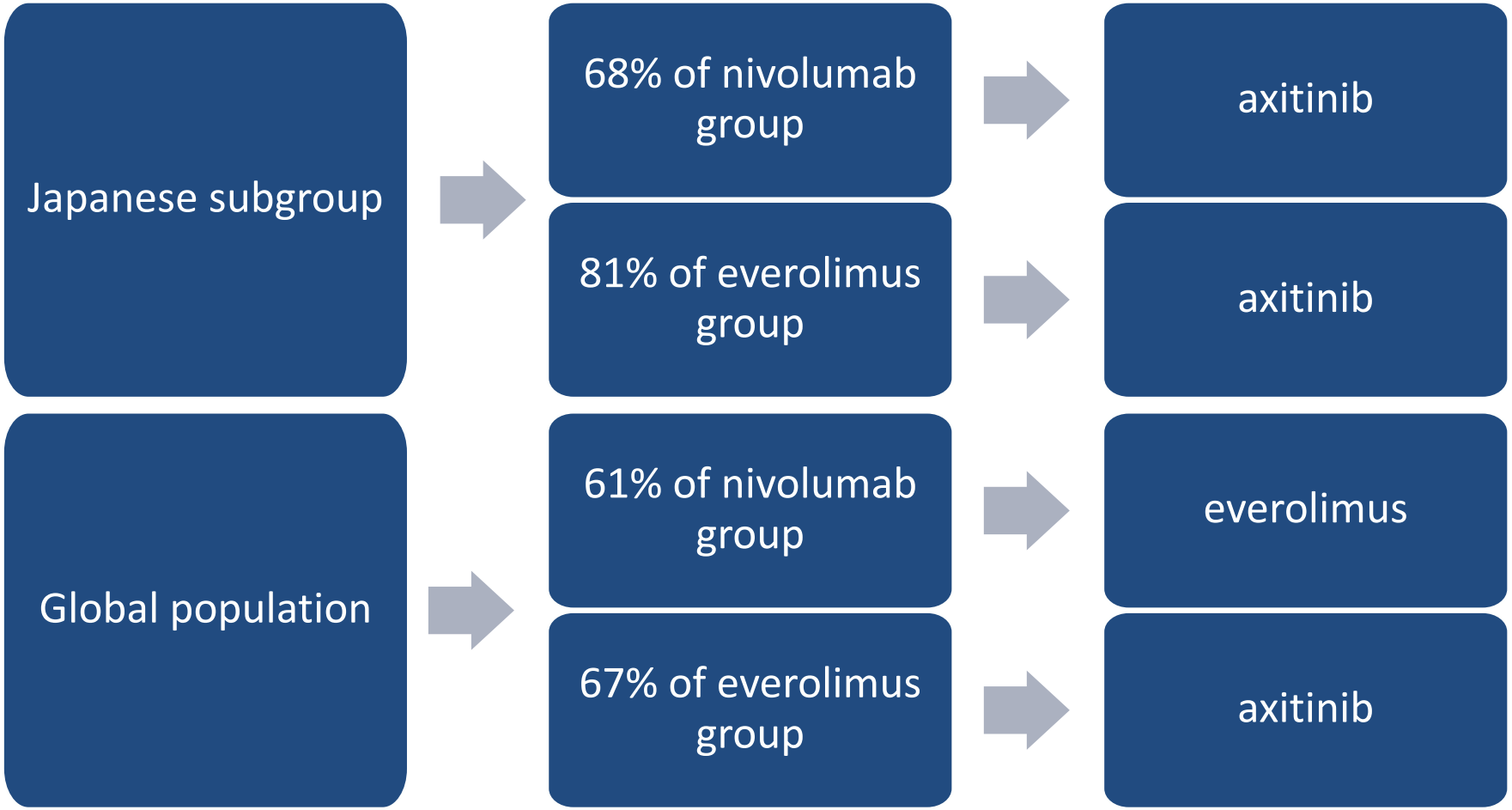
There were differences in rates of starting subsequent therapy in the Japanese subgroup



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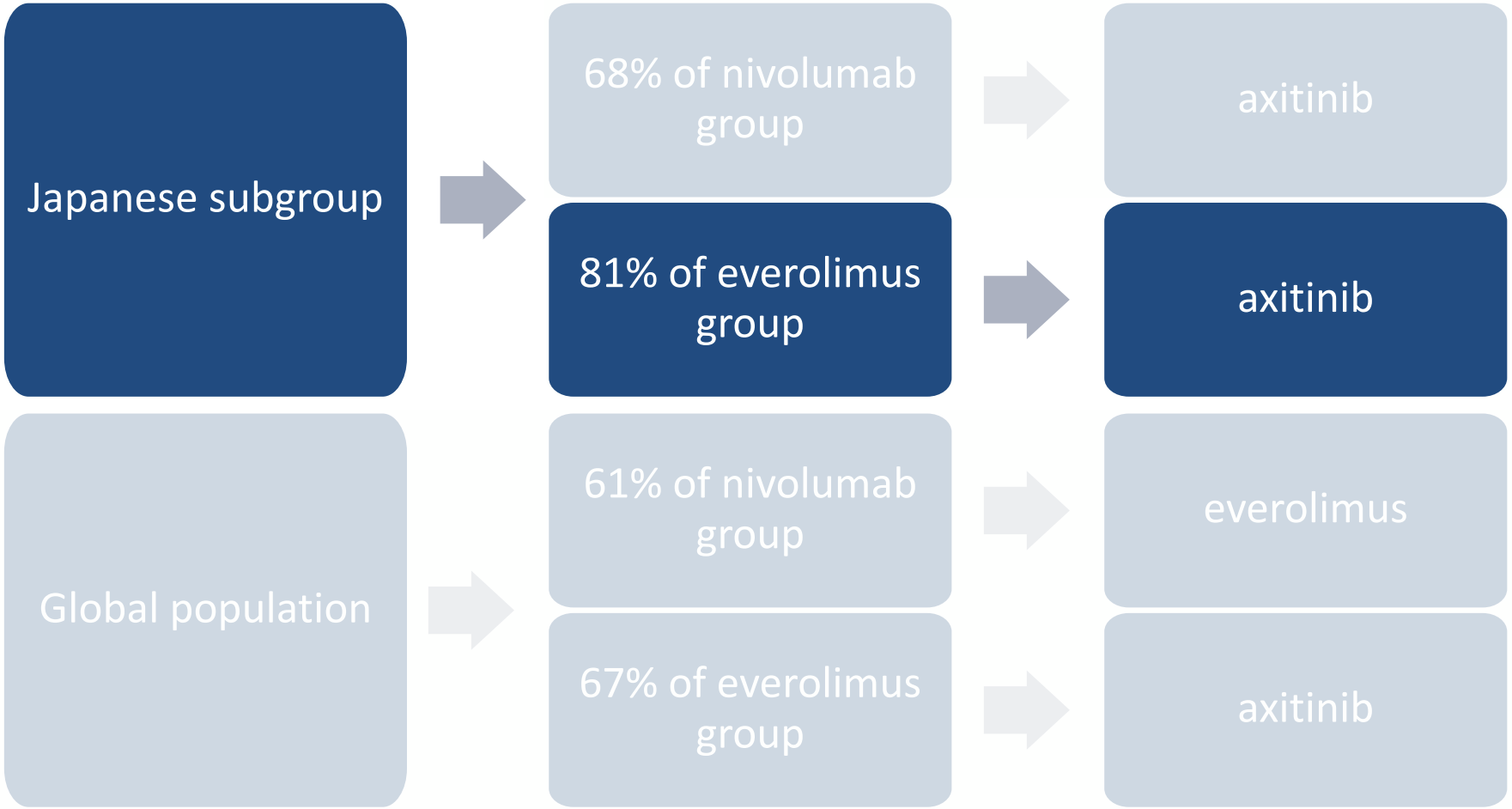

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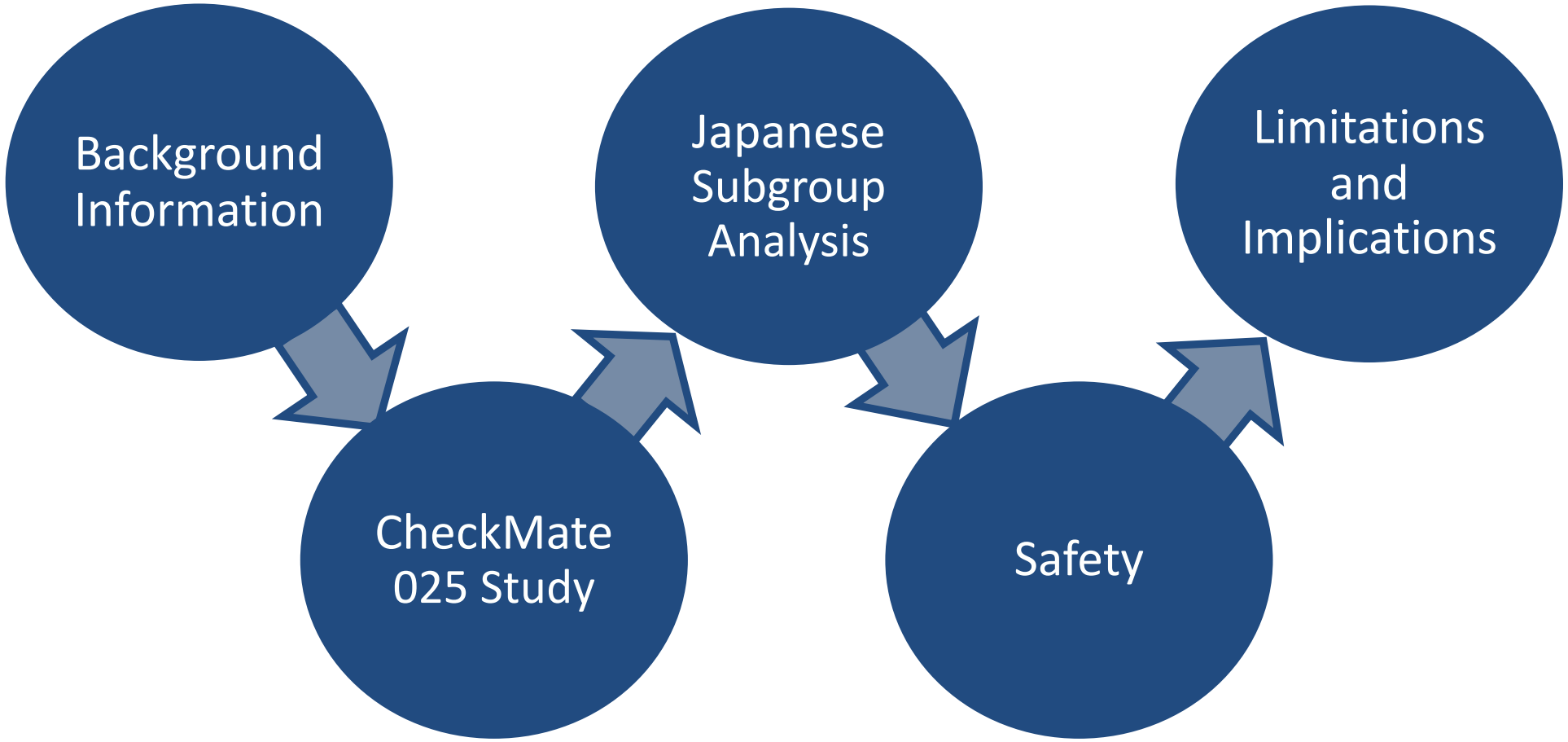
Study limitations affect generalizability



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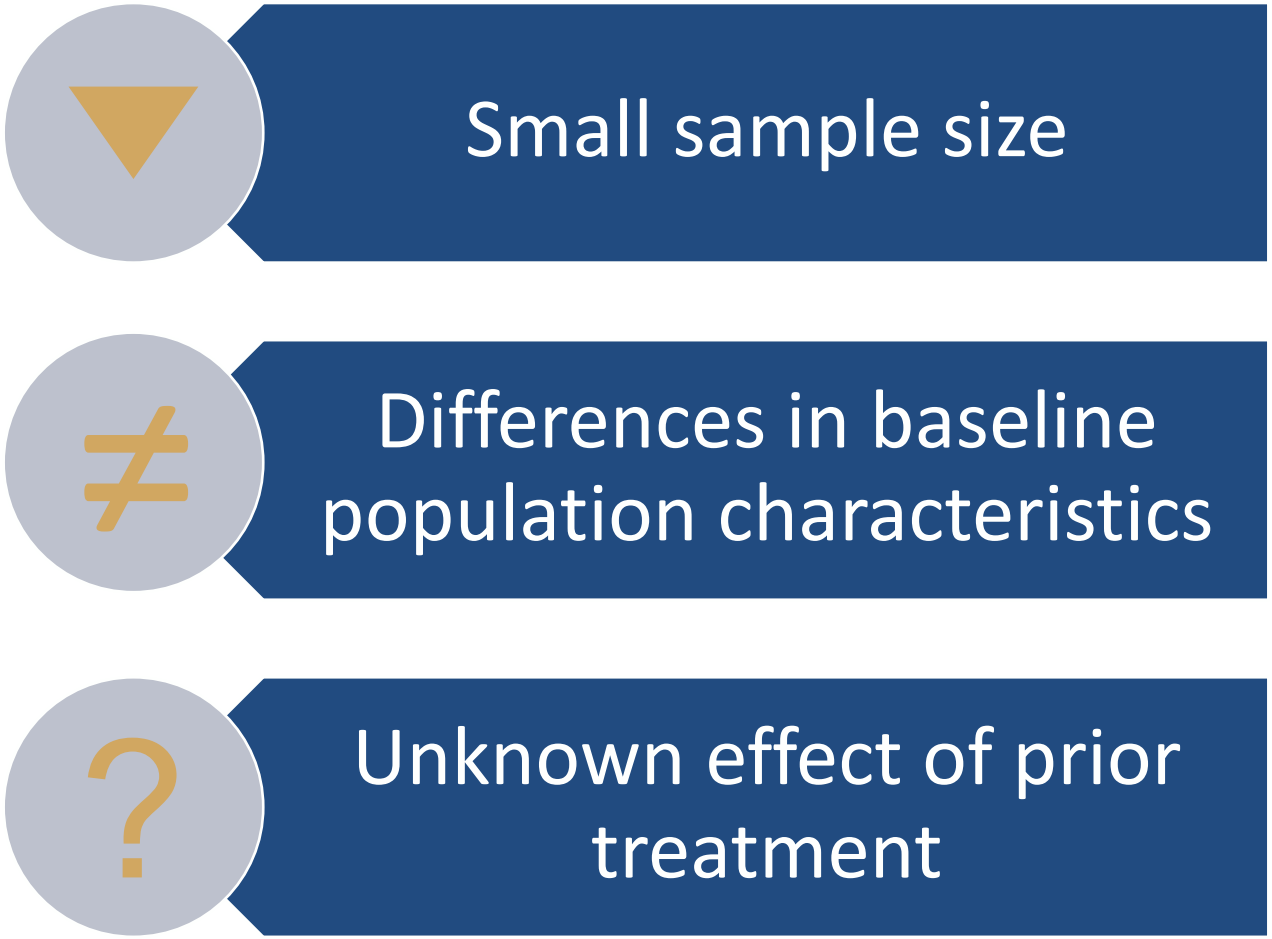

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Given the differences in outcomes in a Japanese subgroup, future studies of renal cell carcinoma treatment should include additional Japanese participants and include dedicated analysis of these participants.

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