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Background

- There are limited data to understand the activity of cabozantinib (CABO) as second line (2L) therapy post ipilimumab-nivolumab (IPI-NIVO) or immuno-oncology/vascular endothelial growth factor inhibitor combinations (IOVE).
- The activity of subsequent 3L approved therapies post CABO has not been established.

Methods

- IMDC database
- All patients who received 2L CABO, or any 3L therapy
- Outcomes of interest for 2L CABO:
 - Overall response rate (ORR)
 - Time to treatment failure (TTF)
 - Overall survival (OS)
- Outcomes of interest for any 3L therapy post 2L CABO:
 - Overall response rate (ORR)
 - Time to treatment failure (TTF)
 - Overall survival (OS)

Results

- 364 patients with mRCC received 2L CABO (78 post IPI-NIVO, 46 post IOVE, 222 post 1L other)
- Of the entire cohort, 12.6%, 62.6% and 24.8% were IMDC favourable, intermediate and poor risk, respectively. 84% had clear cell histology, 18.5% had a sarcomatoid component and 38.3% had bone metastases at diagnosis.
- Outcomes for patients that received 2L CABO, stratified by 1L therapy are outlined in the table, followed by outcomes for patients that received subsequent 3L therapy post 2L CABO.
- After adjustment for IMDC criteria, the HR for 2L CABO OS and TTF for IOVE vs IPI-NIVO were 1.73 (95% CI 0.83-3.62 p=0.14) and 1.62 (0.89-2.95 p=0.11), respectively.

Conclusions

There is clinically meaningful activity of CABO post IPI-NIVO, IOVE and other standard 1L approved therapies.

Clinical outcomes are similar irrespective of 1L therapy. Approved systemic therapies post CABO, mainly single agent VEGF inhibitors also have activity

These are real world benchmarks with which to counsel our patients when using single agent CABO.

Table 1: Outcomes

	Median TTF months (95% CI)	Median OS months (95% CI)	1 Year Treatment Failure Free	1 Year OS	Overall Response Rate
CABO post 1L ALL N=346	7.59 (6.61 - 8.98)	18.12 (15.42 – 24.10)	34.3%	63.5%	26.2% 70/268
CABO post 1L IPI-NIVO N=78	6.90 (6.05 – NE)	21.44 (12.07 – NE)	34.1%	66.6%	26.4% 14/53
CABO post 1L IOVE N=46	5.72 (4.41 – NE)	15.68 (9.27 – NE)	26.8%	54.3%	32.5% 13/40
CABO post 1L OTHER N=222	7.96 (6.81 – 9.63)	18.41 (14.99 – 25.78)	35.7%	63.5%	23.9% 43/180
Outcomes for patients that received 3L therapy post 2L CABO					
Post 2L CABO N=125	3.22 (2.76-5.82)	10.92 (9.44 – 20.02)	19.9%	48.4%	13.3% 12/90

Figure 2: OS in 2L CABO stratified by 1L Therapy

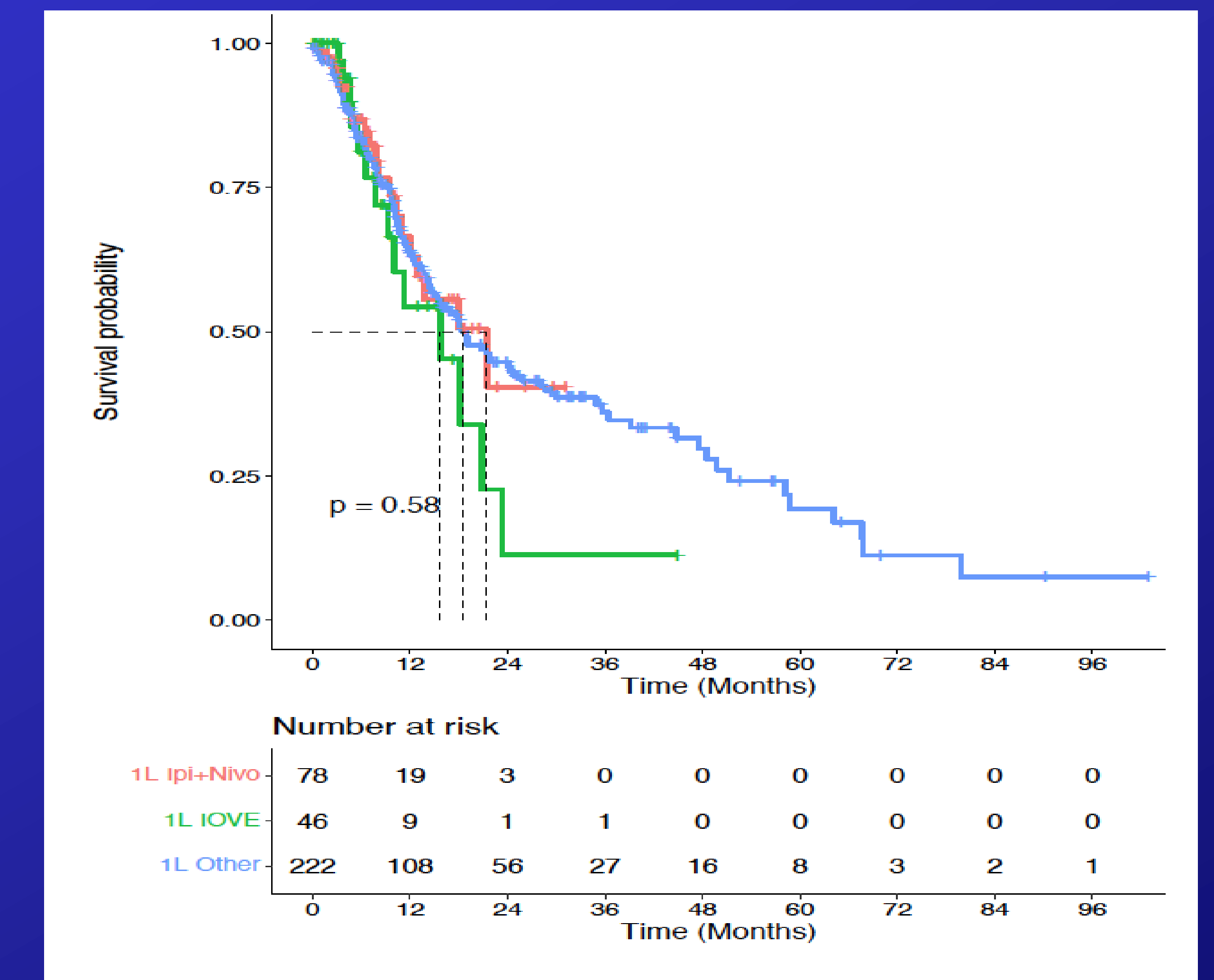
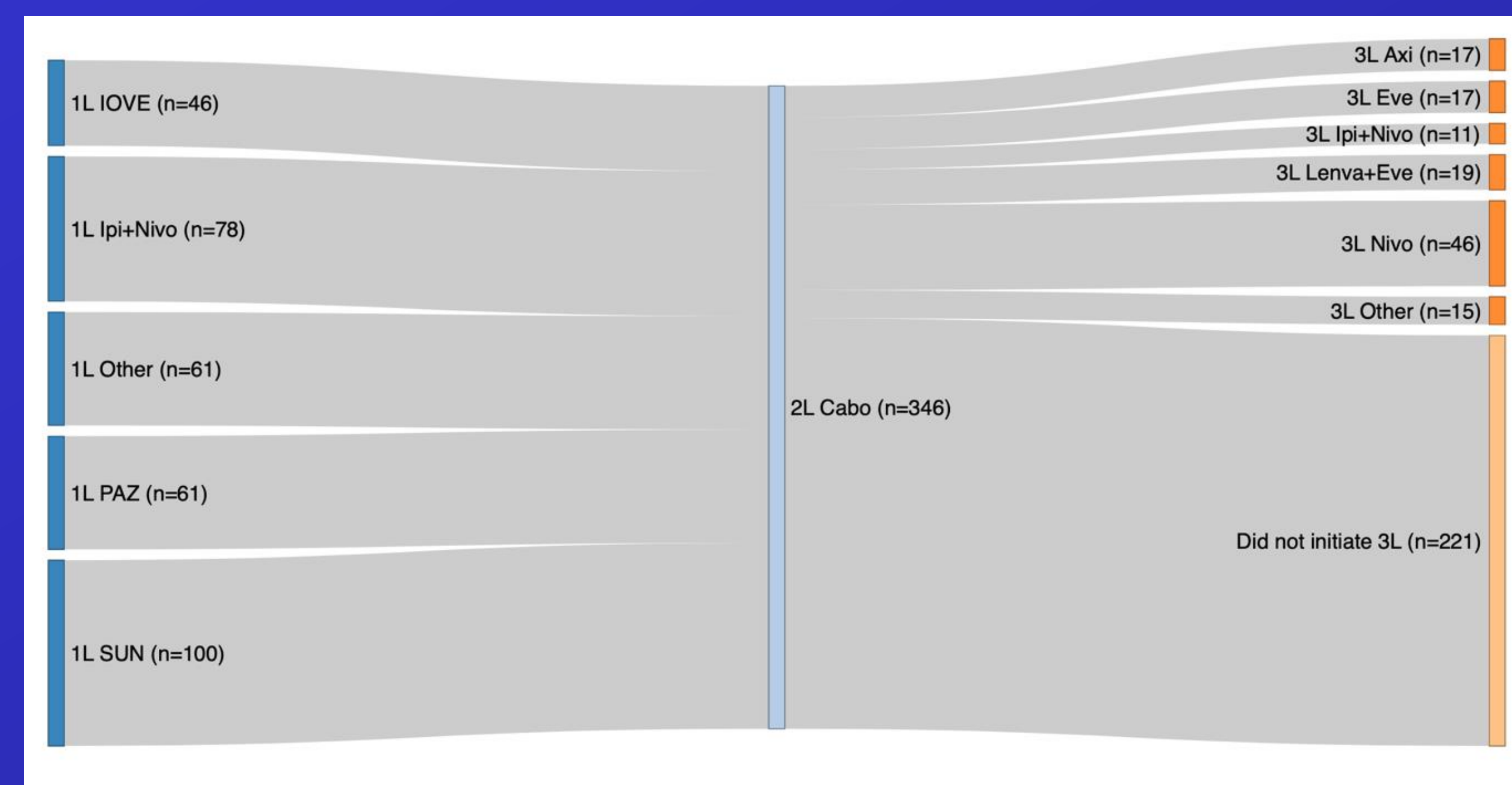


Figure 3: Sankey Diagram outlining Rx sequence for all 2L CABO patients



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