

## Vivli Results Report Form

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**Vivli Data Request ID:** 00007874

**Title of Data Request:** Addressing the synergistic effect of metformin in patients with Pancreatic neuroendocrine tumors treated with sunitinib: a post-hoc analysis from the main pivotal trials

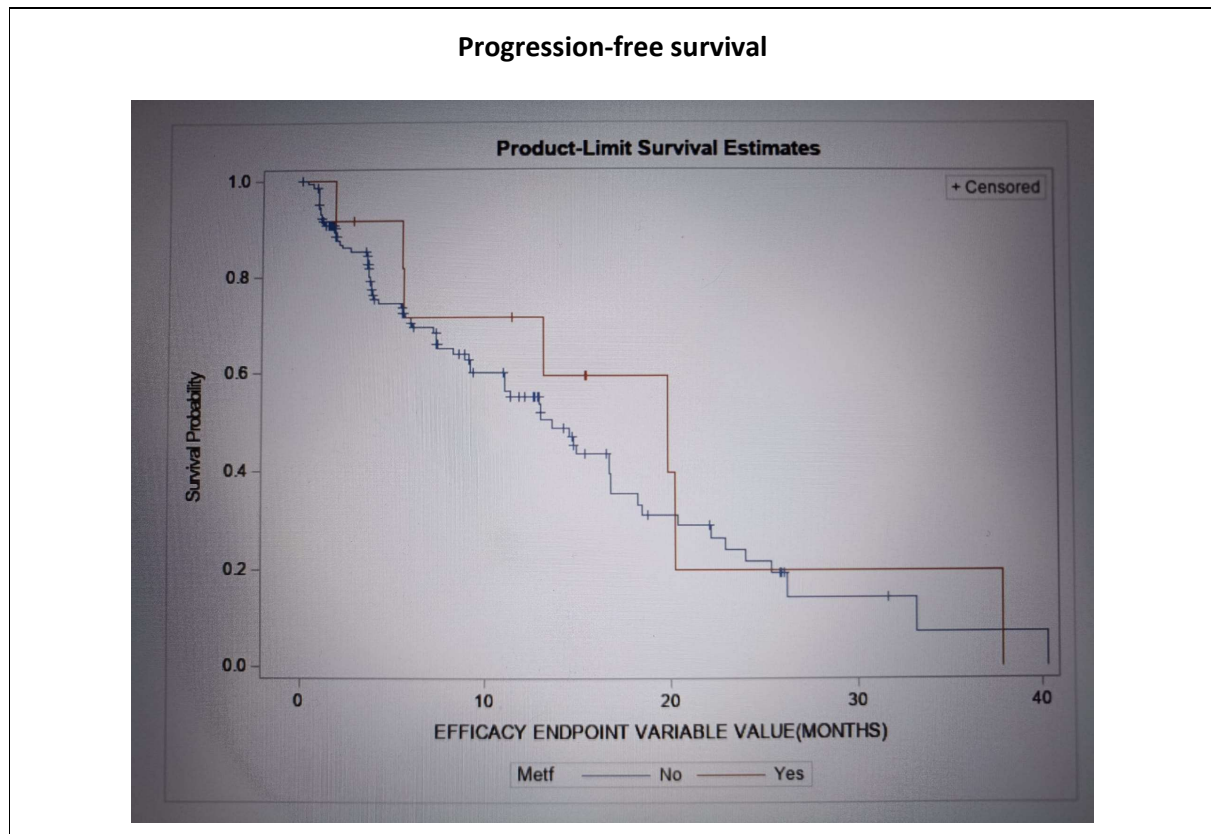
**Date:** 26-Jun-2023

Unfortunately, we were unable to bring our analysis to completion due to the following reasons:

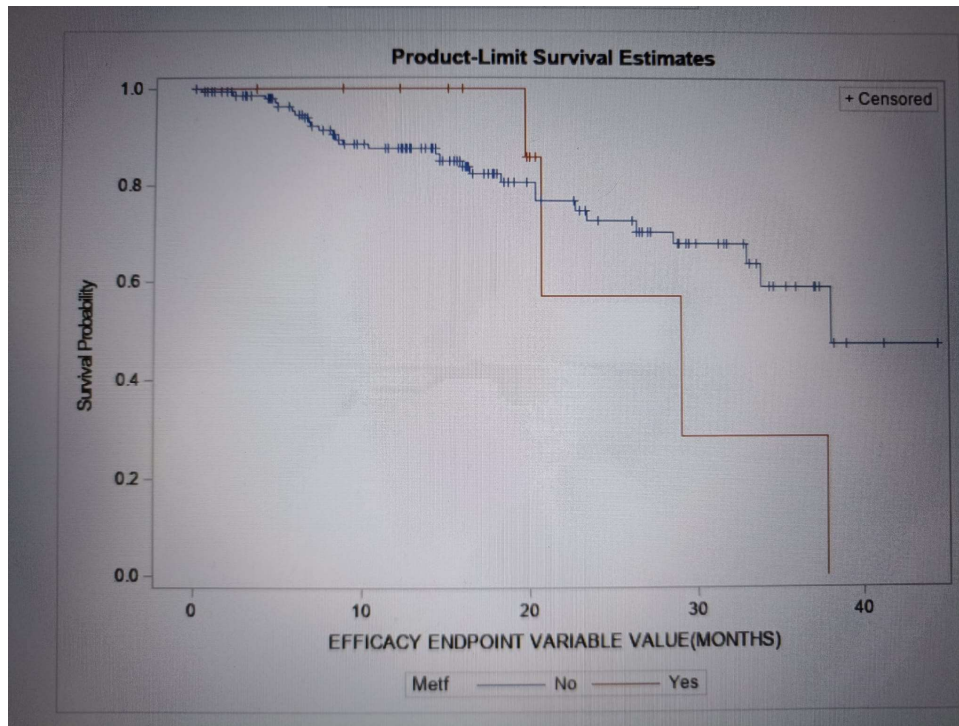
- because of the equivocal classification of patients with or w/o diabetes, we decided to dichotomize the study population into “metformin users” and “non-metformin users”
- We could not use any data from Phase II (Kulke 2008) dataset, since we know that there were three metformin users in the dataset (thanks to your response to our inquiry: “Three patients (metformin users) were hidden by low frequency redaction in the “conmeds” dataset”), but we don’t know who they were and, consequently, if they developed or not the events of interest.
- once having dichotomized the patients, we found that the number of “metformin users” (n = 12) was lower than the original sample size calculated in the statistical plan (n = 19)
- Although we had to exclude the Phase II patients, we tried to perform our analyses, without reaching any conclusive results: there was a weak trend indicating a better PFS for the metformin users and, conversely, a weak trend indicating a worse OS in the same group (no statistical significance).

Below you can find a table and two figures summarizing the results:

	Phase II (Kulke 2008)	Phase III (Raymond 2011)	Phase IV (Raymond 2018)	Phase III + Phase IV			
<b>PFS</b>	<b>PFS events</b>	<b>PFS events</b>	<b>PFS events</b>	<b>PFS events</b>	<b>HR (95% CI)</b>	<b>P-value</b>	<b>Median PFS (95% CI)</b>
<b>Metformin No</b>	?	27 / 81 (33%)	43 / 68 (63%)	70 / 149 (47%)	Ref.		14 (11-17)
<b>Metformin Yes</b>	?	3 / 5 (60%)	4 / 7 (57%)	7 / 12 (58%)	0.77 (0.35- 1.69)	0.51	20 (6-38)
<b>OS</b>	<b>OS events</b>	<b>OS events</b>	<b>OS events</b>	<b>OS events</b>	<b>HR (95% CI)</b>		<b>Median OS (95% CI)</b>
<b>Metformin No</b>	?	8 / 81 (10%)	21 / 68 (31%)	29 / 149 (19%)	Ref.		38 (33-)
<b>Metformin Yes</b>	?	1 / 5 (20%)	3 / 7 (43%)	4 / 12 (33%)	1.46 (0.51- 4.19)	0.48	29 (20-38)



### Overall survival



Therefore, due the inconclusive findings, we do not believe to have publishable results.