

To reviewer A:

Thank you for your suggestions.

To reviewer B:

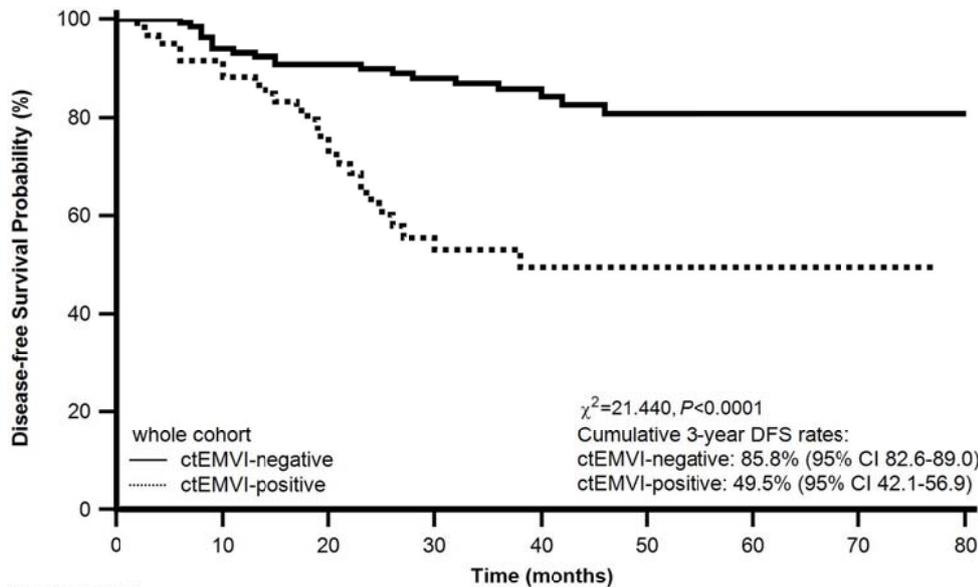
Thank you for your suggestions.

Comment 1: "I suggest including data on chemotherapy regimen given to patients submitted to adjuvant chemotherapy (results pg 12-13). Were all those patients stage III or even stage II at the diagnosis?"

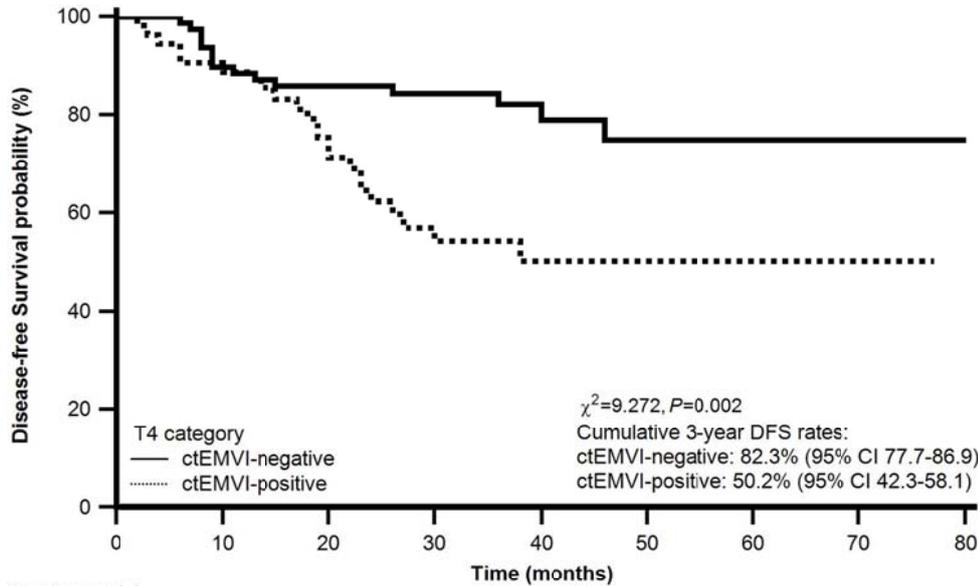
Response 1: We mentioned the data on patients with chemotherapy at the beginning of RESULTS (page 10-11). "121 patients had adjuvant chemotherapy after surgery including 44 stage II patients and 77 stage III patients."

Comment 2: Survival analysis paragraph is difficult to read. Please, include those results into a table and report in the paragraph only what is different among the analytical groups."

Response 2: We rearranged and simplified the survival analysis paragraph and added those results into the figure legends, as shown in the following figures.

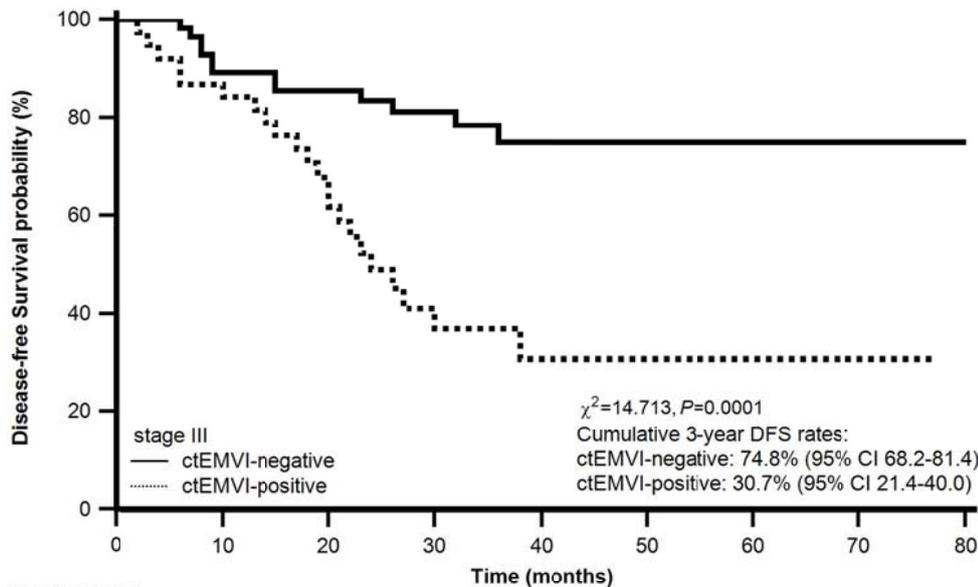


Number at risk									
Group: ctEMVI-negative									
	134	123	112	87	54	36	16	5	0
Group: ctEMVI-positive									
	60	53	39	22	13	10	7	2	0



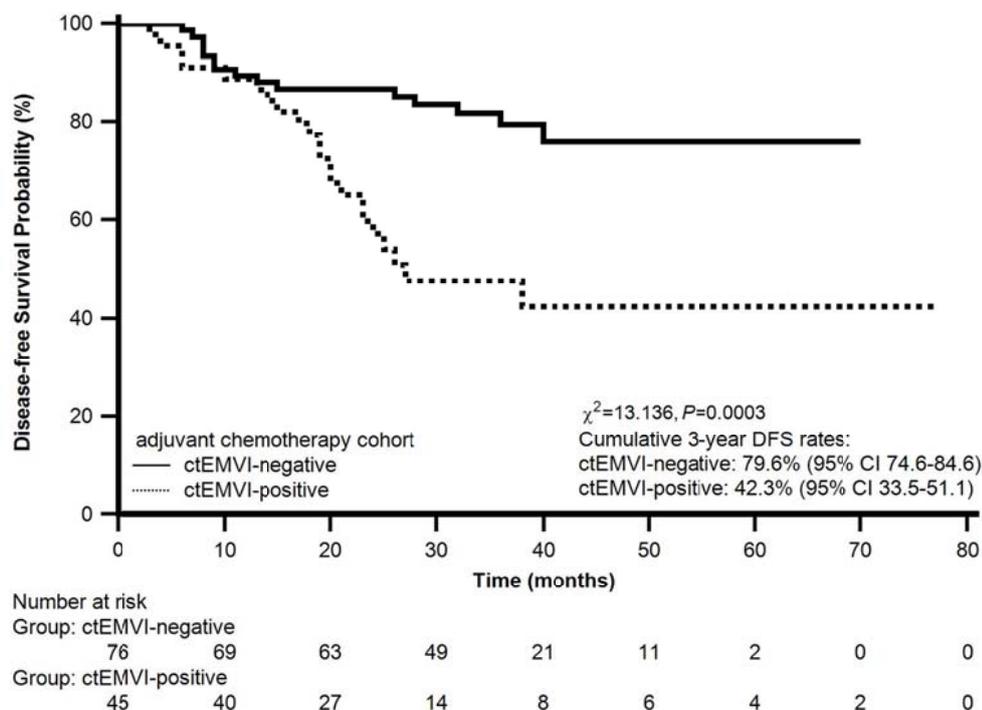
Number at risk

Group: ctEMVI-negative	80	70	64	50	25	14	7	3	0
Group: ctEMVI-positive	54	48	35	20	11	8	5	1	0



Number at risk

Group: ctEMVI-negative	56	49	43	32	17	10	2	1	0
Group: ctEMVI-positive	38	32	21	9	5	4	3	2	0



Comment 3: I suggest restyling the discussion.

Response 3: We appreciate this comment, but we were unsure what was specifically meant by “restyling” and thus unsure of what changes we should make. We did carefully reevaluate the discussion and revised it accordingly. We also asked for a native English speaker to review the whole paper again to check our use of the English language.

We also made the following revisions:

1. Added the ESPS manuscript NO.
2. Made some minor revise in the Abstract and Main text.
3. Capitalized the first letter of Key Words.
4. Made some minor revise on page 11.
 - (1) Added the sentence “Of the 134 T4 patients, ctEMVI was observed in 54 patients (40.3%, 54/134).” in the “Incidence of ctEMVI” paragraph.
 - (2) Added “the T4 subgroup” and “within the T4 subgroup” in the “Progressive Events Rates” paragraph.
5. According to the advice of reviewer B (reviewer’s code: 03258480), we put the complex and repeated results into the Figure 3A-D, and added clear and simple results in the “Survival analysis” paragraph.

“Based on the Kaplan-Meier method, the survival curves were significantly different between ctEMVI-positive and ctEMVI-negative patients in the whole cohort, the T4 subgroup, the stage III



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subgroup, and the adjuvant chemotherapy subgroup ($p < 0.01$). The cumulative 3-year DFS rates for ctEMVI-positive and ctEMVI-negative patients are shown in Picture 3A-D. "(page 12)

6. Added "COMMENTS".

7. Changed Figure 3A-D as mentioned.

8. Added an "adjuvant chemotherapy" column in Tables 2 and 3 and made minor revise in Table 2.

9. Replaced the word "PFS" with "DFS" in table 4.

10. Regarding About the certificate, we asked for the iCoreMed company to review our revised manuscript again as they had also reviewed the previous version. They double check the language again. They provided a new certificate for the revised version.