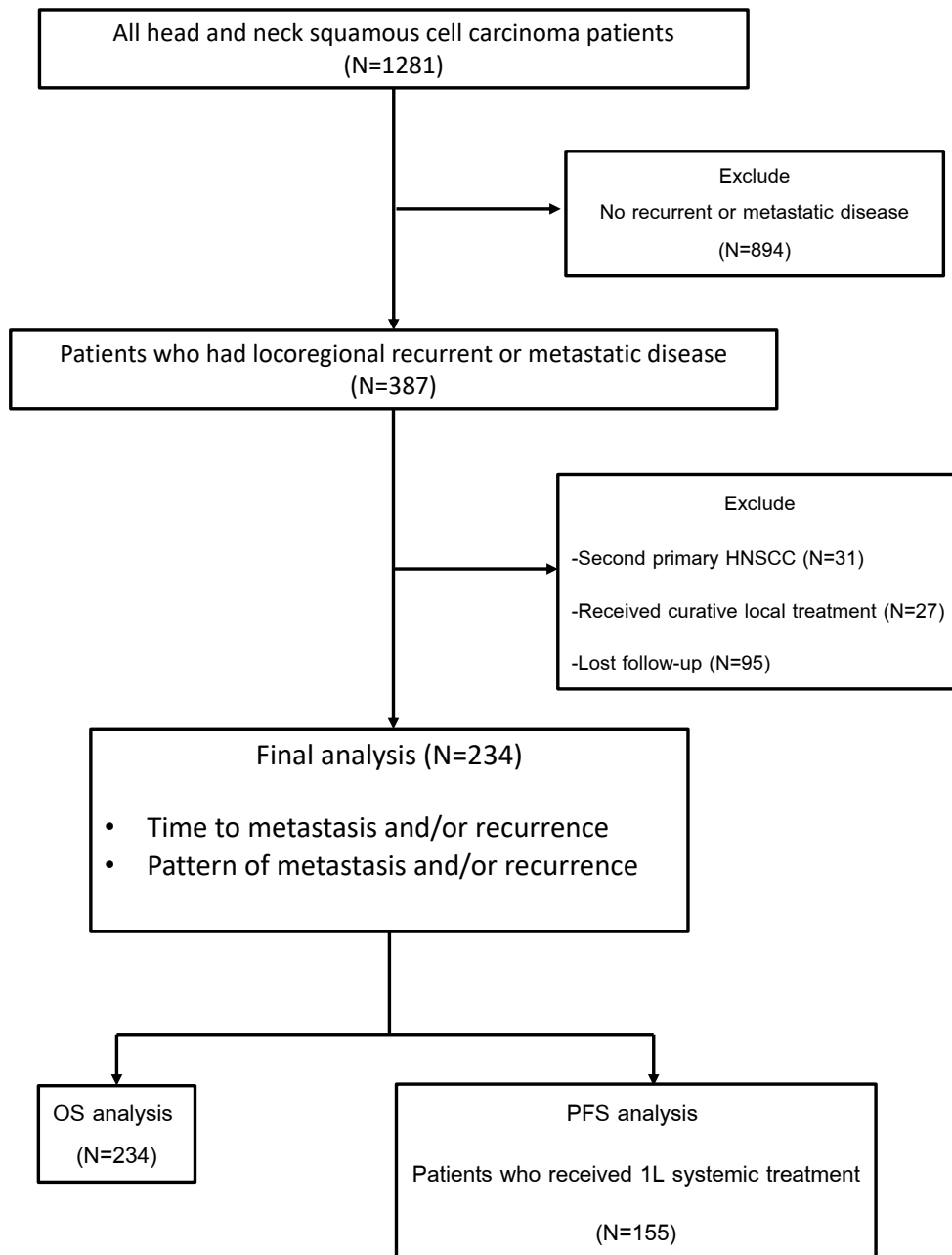
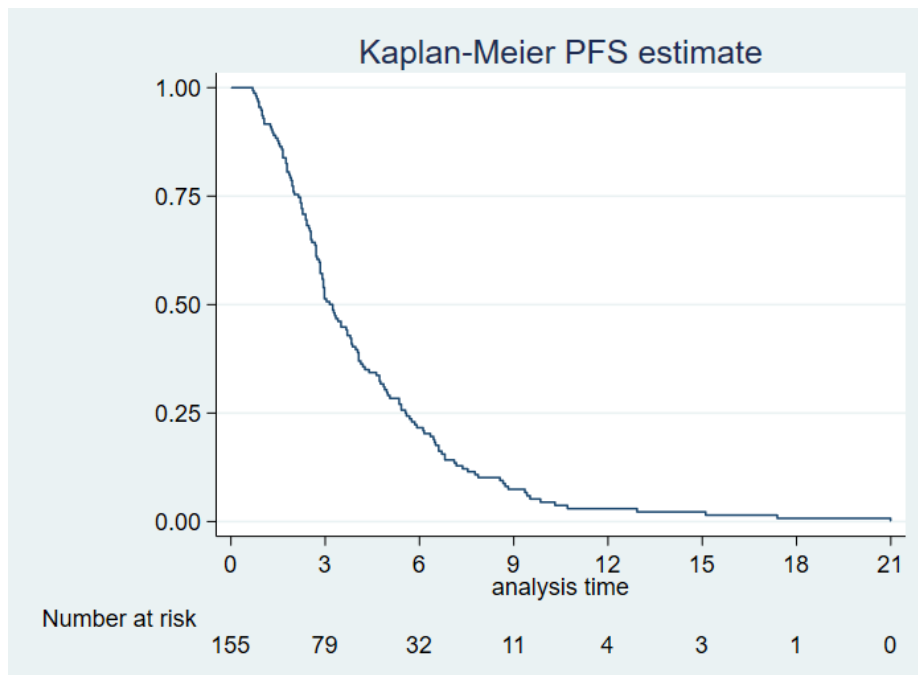


Supplement 1: Consort diagram

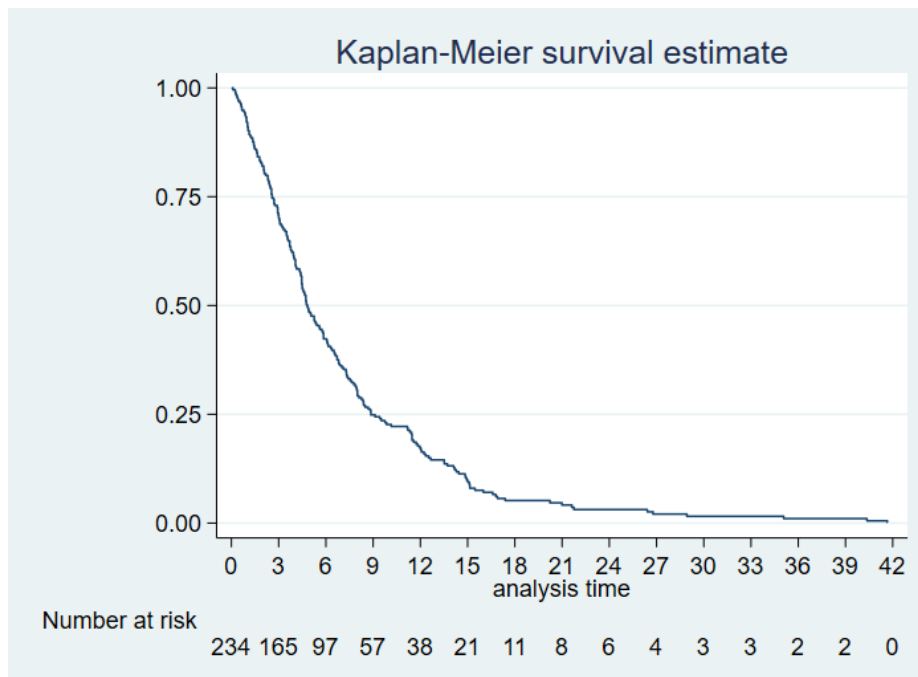


Supplement 2: PFS of all RM-HNSCC patients



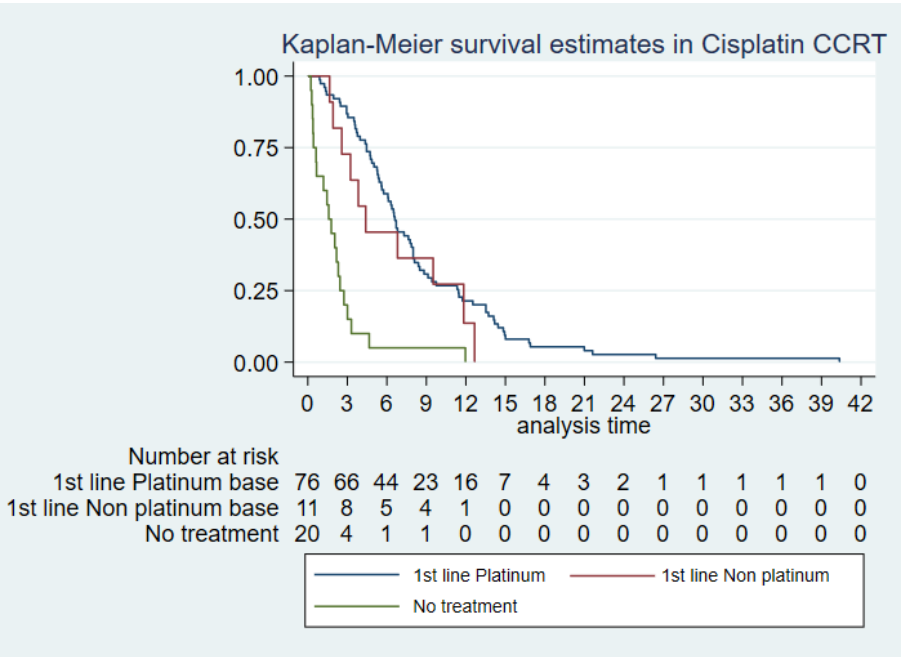
Median PFS = 3.2 (2.8-3.7) months

Supplement 3: OS of all RM-HNSCC patients



Median OS = 4.8 (4.5-5.8) months

Supplement 4: OS of RM-HNSCC patients who previously received cisplatin-based CCRT with 1L systemic treatment by type of regimen.



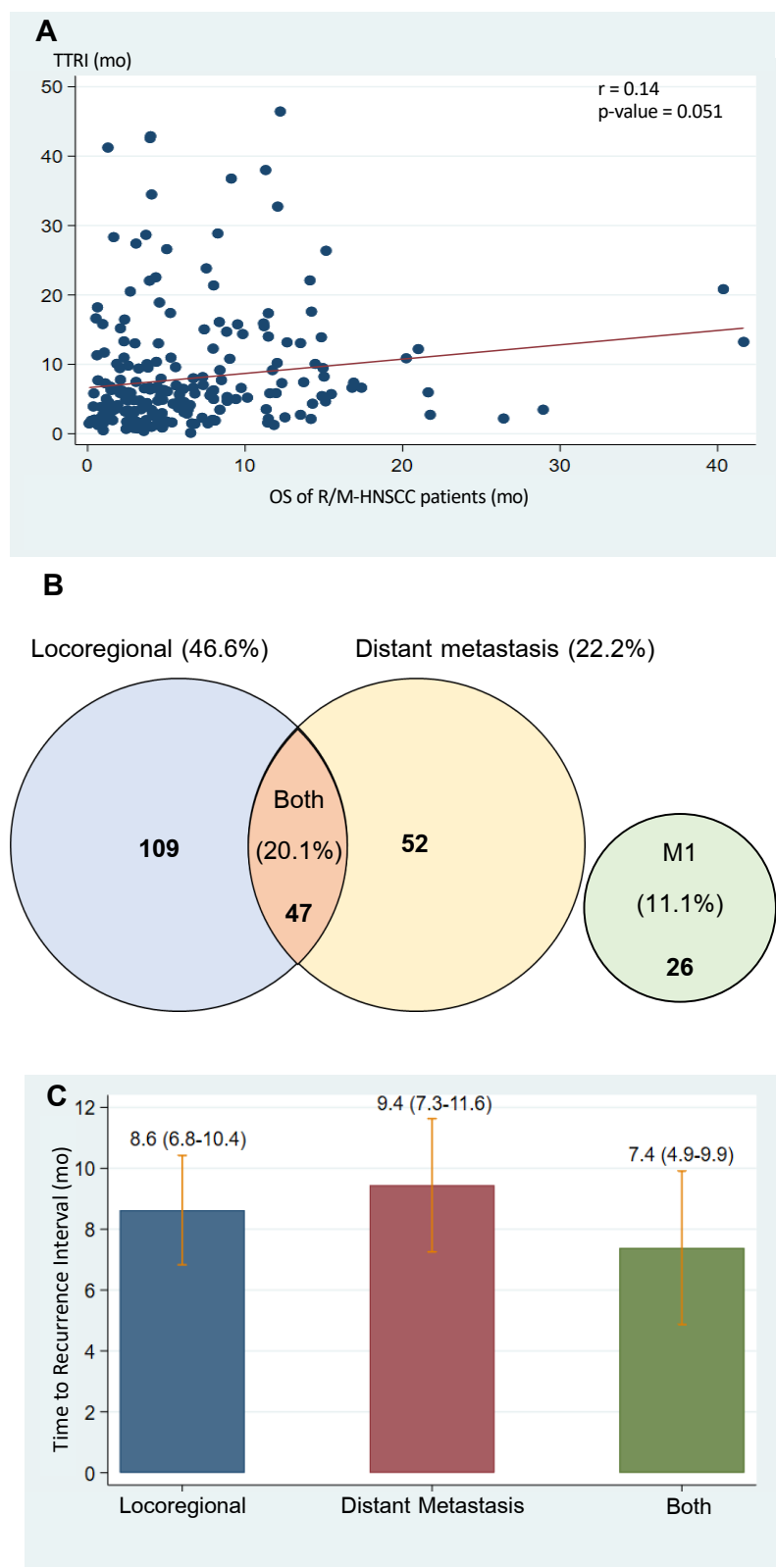
Median OS of 1st line Platinum = 6.6 (5.6-7.9) months

Median OS of 1st line Non platinum = 4.4 (1.9-11.3) months

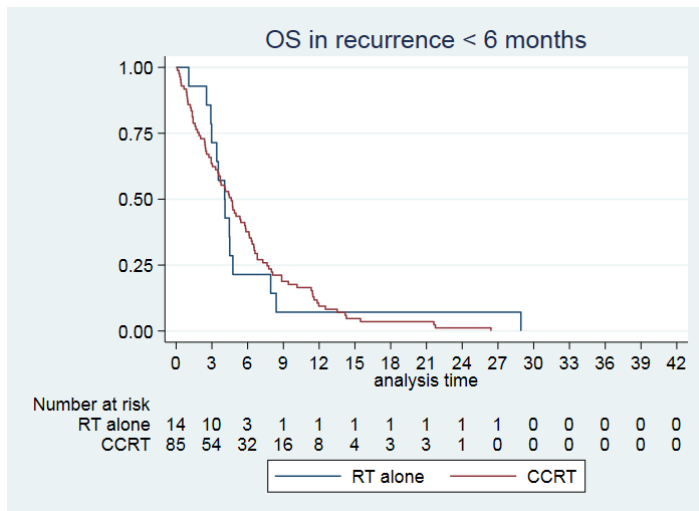
Median OS of No treatment = 1.6 (0.4-2.3) months

P value <0.001

Supplement 5 Scatter plot of time to recurrence interval (TTRI) and OS of RM-HNSCC patients (A); Pattern of recurrence (B); Duration of last definitive treatment to recurrence by pattern of recurrence (C)



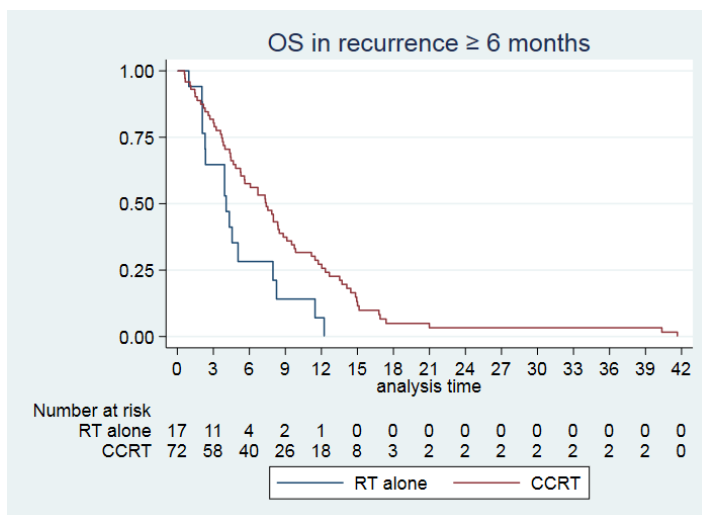
Supplement 6. Impact of TTRI on OS for R/M-HNSCC patients who were previously treated with RT alone or CRT.



CRT = 4.6 (3.3-5.8) months

RT alone = 4.1 (2.9-4.8) months

HR 1.01 (0.56-1.83), $p = 0.964$

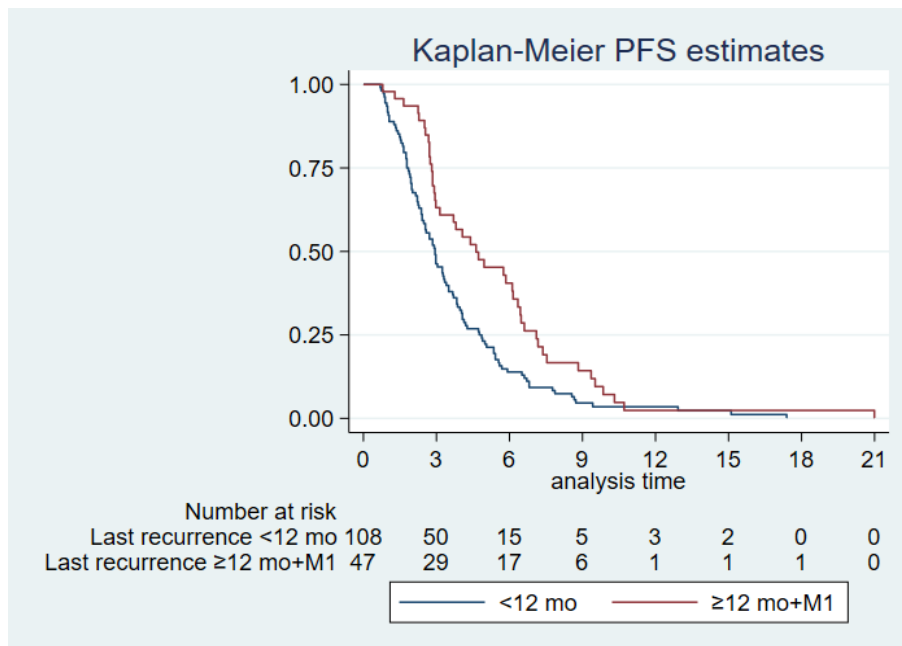


CRT = 7.4 (5.3-8.8) months

RT alone = 4.1 (2.1-8.0) months

HR = 0.48 (0.27-0.84), $p = 0.017$

Supplement 7. PFS of RM-HNSCC patients by duration of recurrent and metastatic disease using TTRI 12 months as a cut-off.

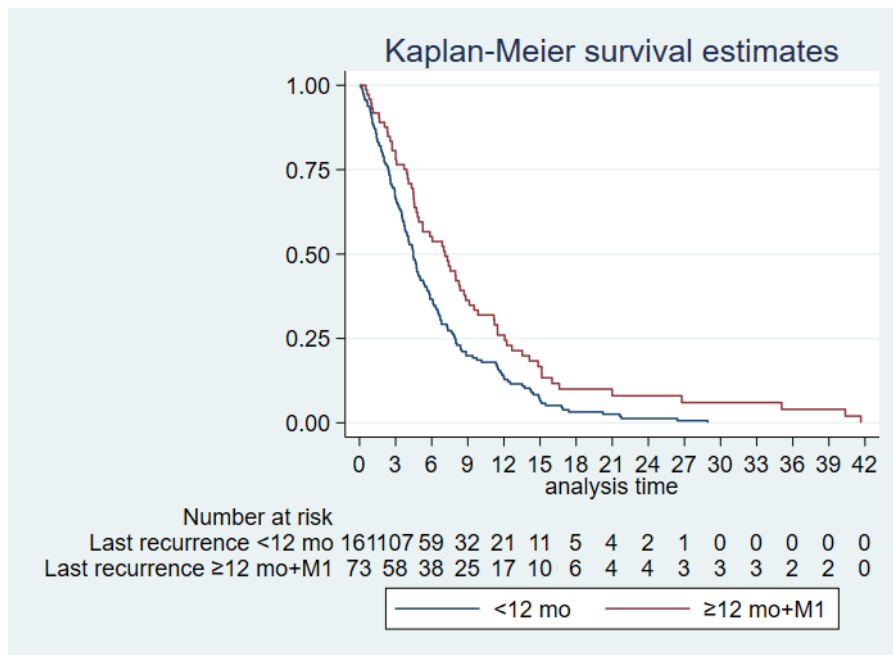


Median PFS TTRI <12 mo = 2.9 (2.4-3.3) months

Median PFS TTRI $\geq$ 12 mo + M1 = 4.6 (2.9-6.1) months

HR = 0.59 (0.41-0.84), p-value = 0.003

Supplement 8 OS RM-HNSCC patients by duration of recurrent and metastatic disease using TTRI 12 months as a cut-off.



Median OS TTRI <12 months = 4.5 (3.8-5.0) months

Median OS TTRI $\geq$ 12 months+M1 = 7.1 (4.8-8.4) months

HR = 0.62 (0.47-0.84), p-value= 0.002