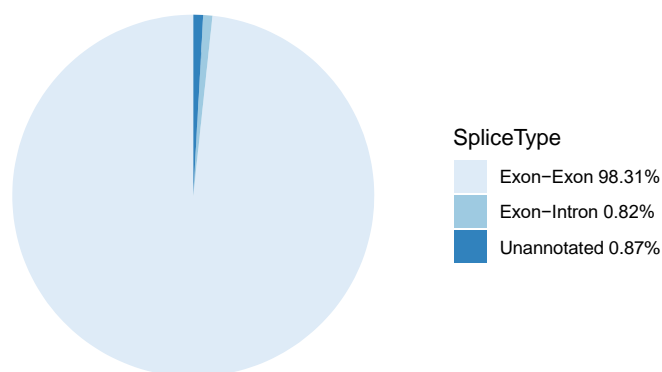
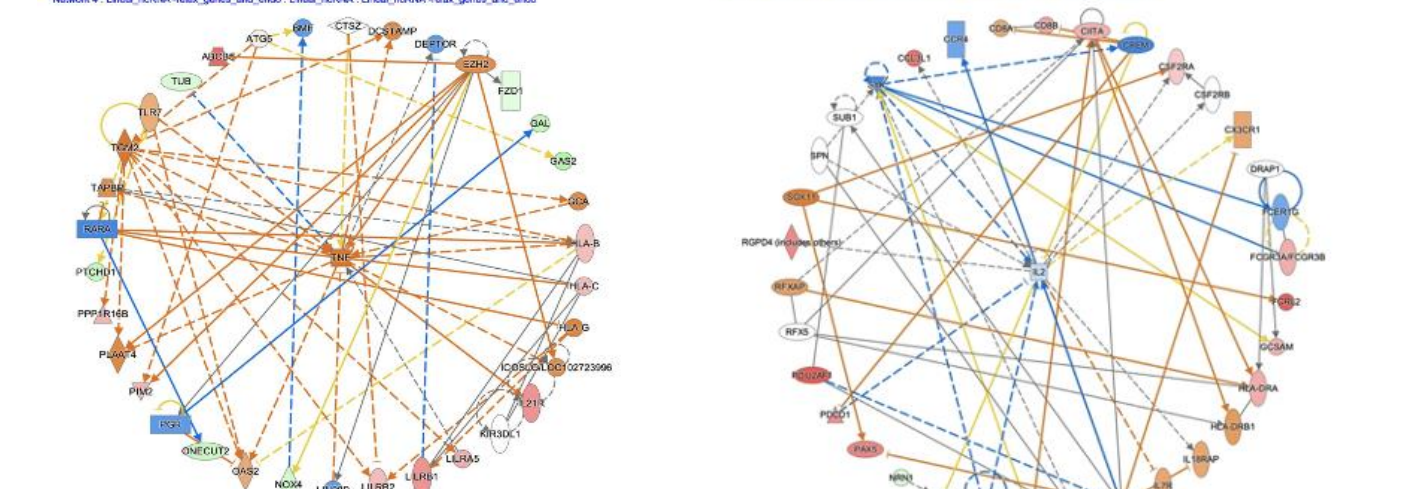


Supplementary Figure S1. RT-PCR validation of *CDR1*. (a) Correlation between ΔCt obtained by real time PCR and TPM generated by RNA-seq. (b) ΔCt of responders and non-responders.



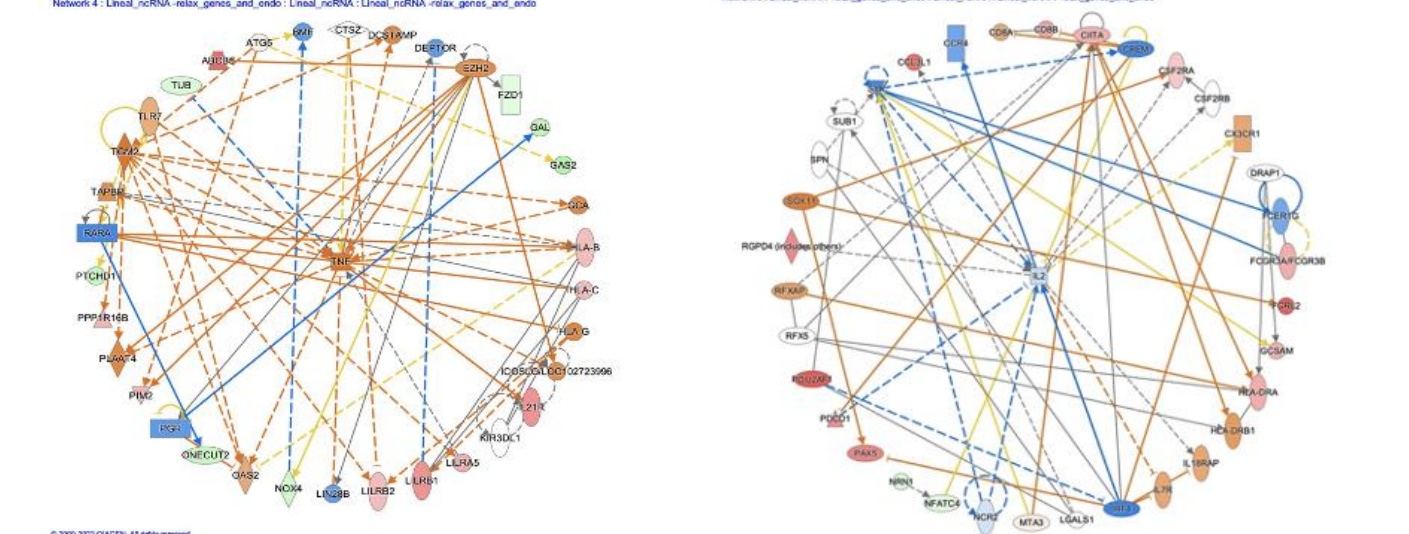
Supplementary Figure S2. CircRNAs exon types. Mapping of circRNAs indicates that 98.3% of identified circRNAs are exon-exon type.

Network 4: *Lineal_ncRNA-relax_genes_and_endo*: *Lineal_ncRNA*: *Lineal_ncRNA-relax_genes_and_endo*

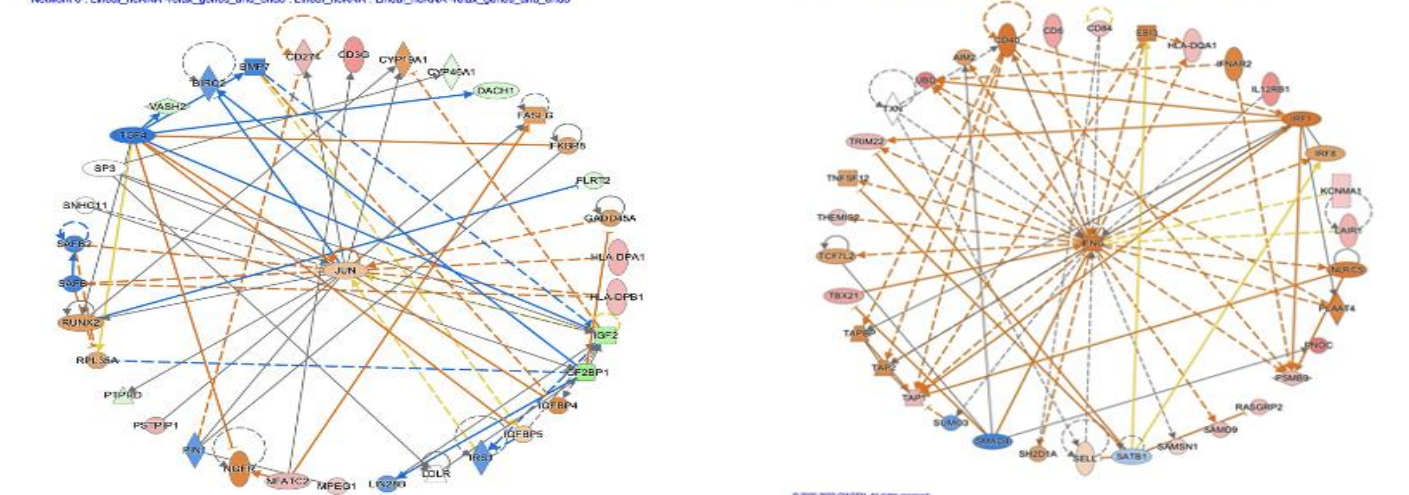


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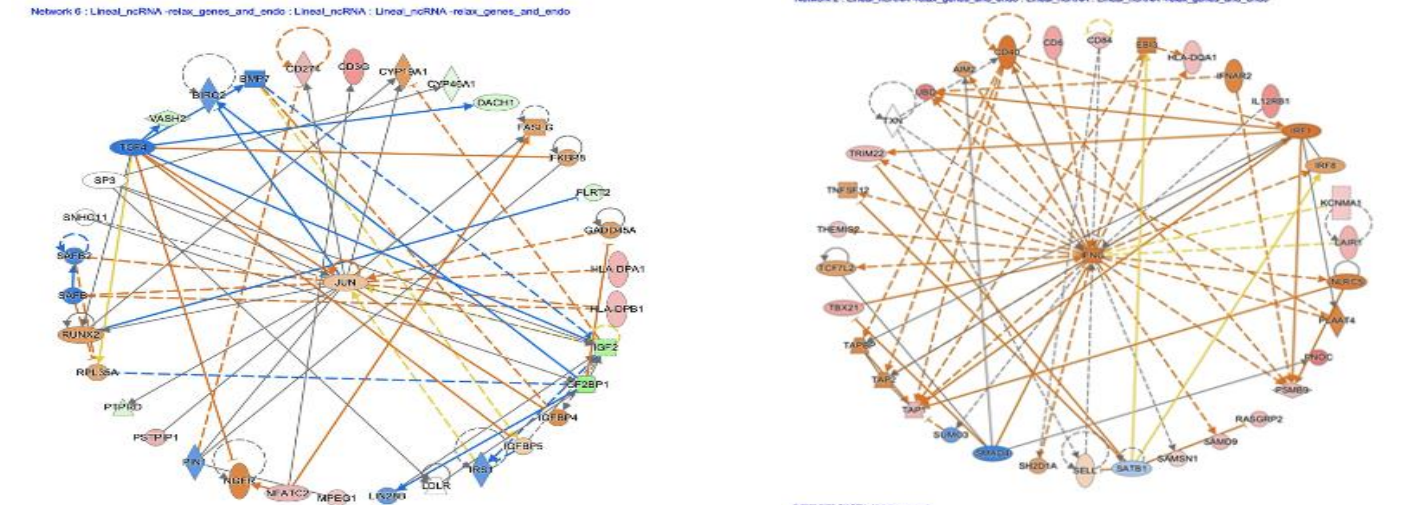
Network 5: Linear ncRNA-relax_genes and endo: Linear ncRNA: Linear ncRNA-relax_genes and endo



Network 6: Linear ncRNA-relax genes and endo: Linear ncRNA: Linear ncRNA-relax genes and endo

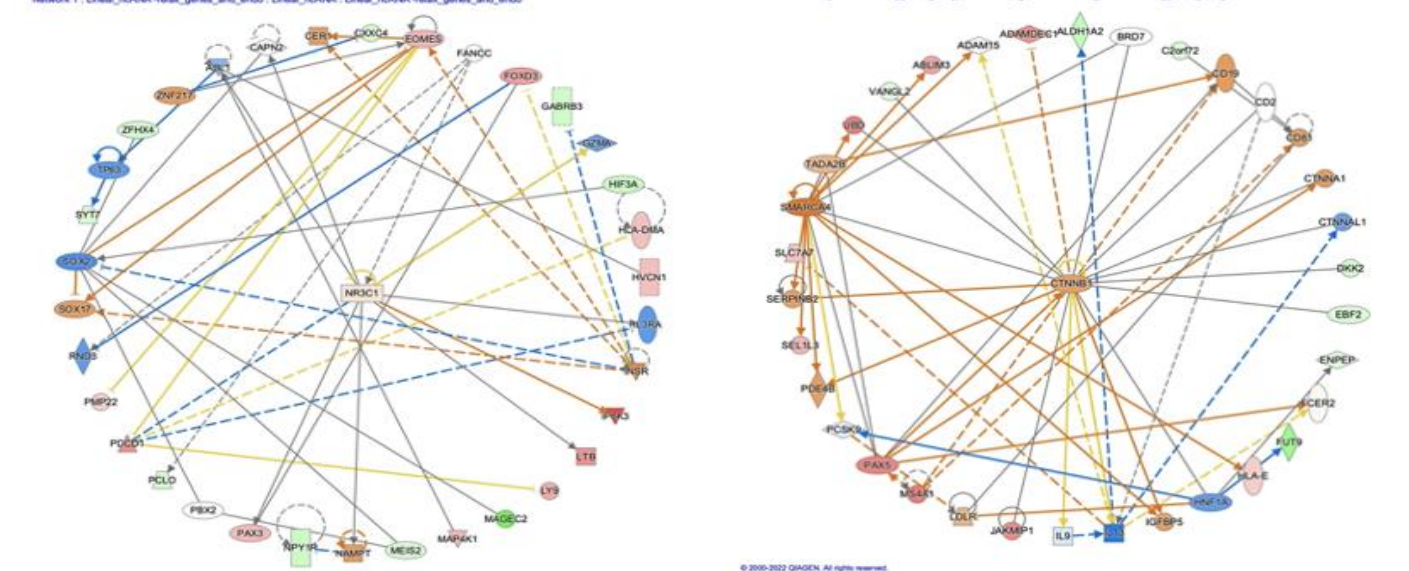


Network 2: Linear ncRNA-relax genes and endo: Linear ncRNA: Linear ncRNA-relax genes and endo

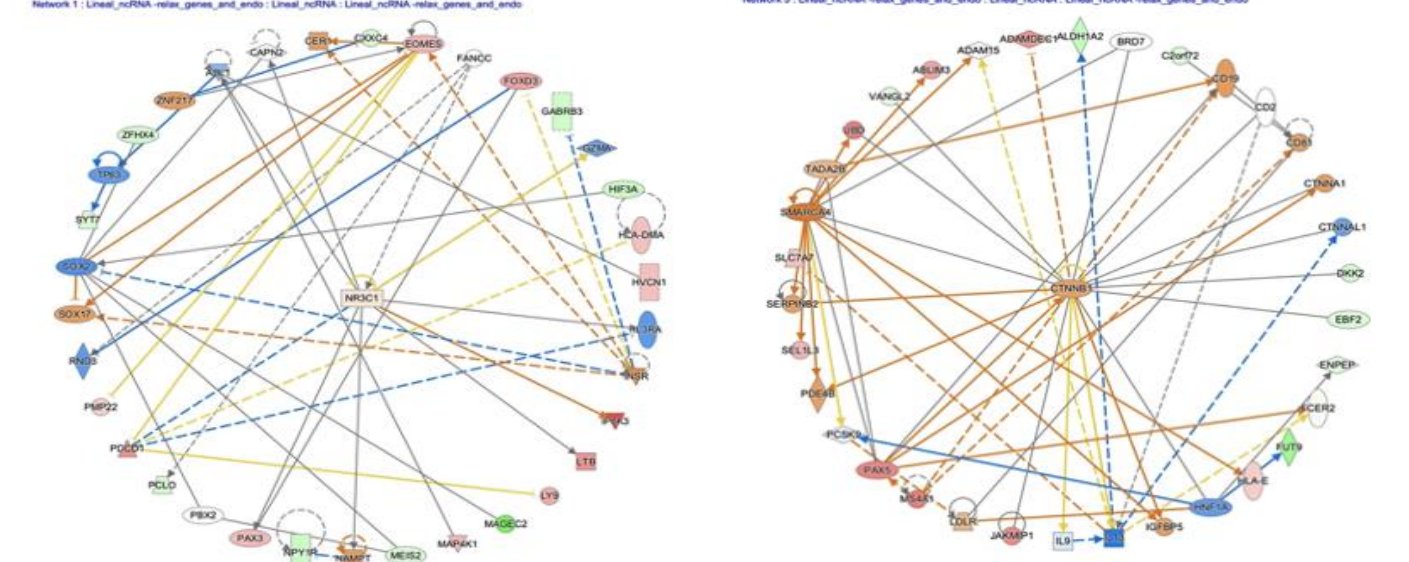


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Network 1: Linear_ncRNA-relax_genes_and_endo: Linear_ncRNA: Linear_ncRNA-relax_genes_and_endo

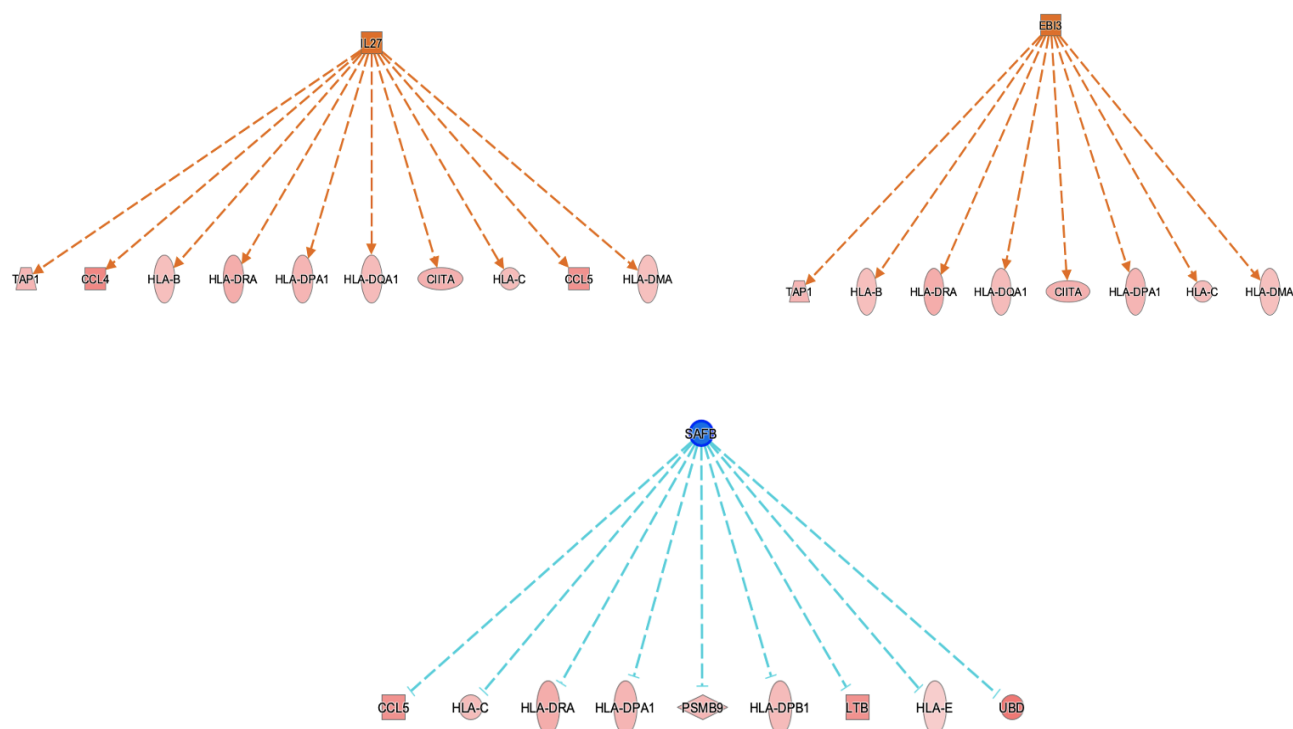


Network 3: Linear ncRNA-relax genes and endo: Linear ncRNA: Linear ncRNA-relax genes and endo



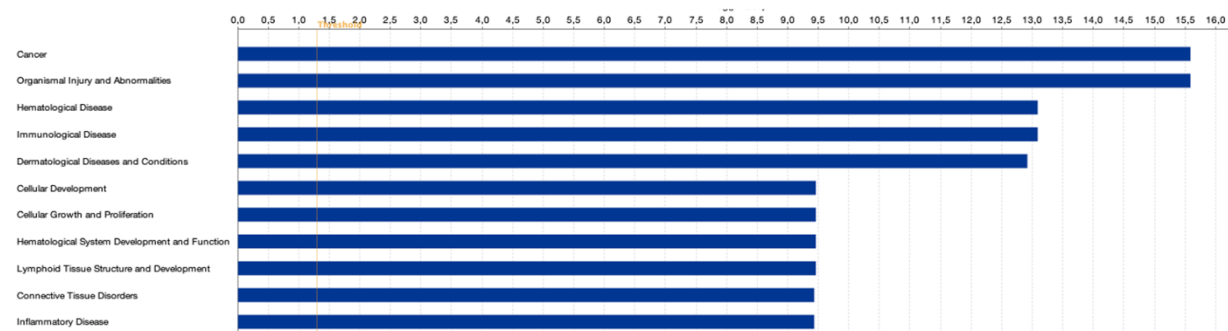
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(b)

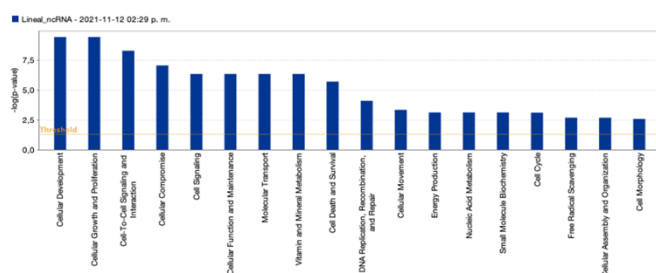


Supplementary Figure S3. Interaction networks and upstream molecules. **(a)** Interaction networks of the main molecules of the differentially expressed mRNAs of the ceRNA network predicted by IPA. **(b)** Main relevant activated upstream molecules are IL27 and EBI3, while SAFB is an important inhibited upstream regulator associated to our ceRNA network.

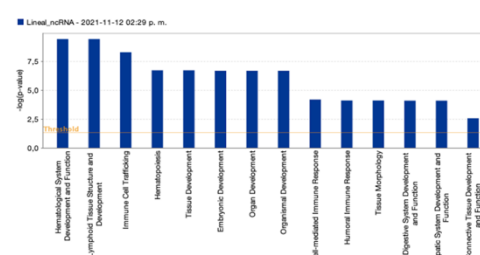
IPA ontology



Molecular and cellular function



Physiological system & physiology



Supplementary Figure S4. Top enriched IPA ontologies and pathways of the molecular and cellular function and the physiological system and physiology.

Supplementary Table S1. Clinical characteristics of 12 CMM patients treated with immunotherapy.

| Variables | Value | Responders | Non-responders | Lost Values |
|--------------------|-----------|------------|----------------|-------------|
| Sex | Female | 5 (62.5%) | 1 (25%) | 0 (0%) |
| | Male | 3 (37.5%) | 3 (75%) | |
| Stage at diagnosis | Stage I | 1 (14.29%) | 0 (0%) | 1 (0.08%) |
| | Stage II | 2 (28.57%) | 2 (50%) | |
| | Stage III | 4 (57.14%) | 0 (0%) | |
| | Stage IV | 0 (0%) | 2 (50%) | |
| Diabetes | No | 7 (87.5%) | 3 (75%) | 0 (0%) |
| | Yes | 0 (0%) | 0 (0%) | |

| | | | | | |
|---------------------------------------|-----------|--------------------|---------------------|------------------|--------|
| | Yes | 2 (16.67%) | 1 (12.5%) | 1 (25%) | |
| Dyslipidemia | | | | | 0 (0%) |
| | No | 9 (75%) | 5 (62.5%) | 4 (100%) | |
| | Yes | 3 (25%) | 3 (37.5%) | 0 (0%) | |
| Hypertension | | | | | 0 (0%) |
| | No | 4 (33.33%) | 2 (25%) | 2 (50%) | |
| | Yes | 8 (66.67%) | 6 (75%) | 2 (50%) | |
| Status | | | | | |
| | Alive | 4 (33.33%) | 4 (50%) | 0 (0%) | |
| | Dead | 8 (66.67%) | 4 (50%) | 4 (100%) | |
| Overall survival time | | 17.26 [0.92–45.97] | 26.49 [10.52–45.97] | 1.84 [0.92–3.28] | 0 (0%) |
| Progression | | | | | |
| | No | 3 (25%) | 3 (37.5%) | 0 (0%) | |
| | Yes | 9 (75%) | 5 (62.5%) | 4 (100%) | |
| Progression-free survival time | | 8.98 [0.52–45.97] | 15.74 [5.9 – 45.97] | 2.08 [0.52–2.33] | 0 (0%) |
| Stage prior to ICB treatment | | | | | |
| | Stage I | 0 (0%) | 0 (0%) | 0 (0%) | |
| | Stage II | 0 (0%) | 0 (0%) | 0 (0%) | |
| | Stage III | 0 (0%) | 0 (0%) | 0 (0%) | |
| | Stage IV | 11 (100%) | 8 (100%) | 4 (100%) | 0 (0%) |
| No. metastasis | | 2 [1–4] | 2.5 [1–4] | 2 [1–3] | 0 (0%) |
| Lung metastasis | | | | | 0 (0%) |

| | | | | |
|--|--------------------|--------------------|---------------------|-----------|
| No | 4 (33.33%) | 1 (12.5%) | 3 (75%) | |
| Yes | 8 (66.67%) | 7 (87.5%) | 1 (25%) | |
| Lymph node metastasis | | | | 0 (0%) |
| No | 4 (33.33%) | 4 (50%) | 0 (0%) | |
| Yes | 8 (66.67%) | 4 (50%) | 4 (100%) | |
| LDH first metastasis (U/L) | 164 [107–498] | 215 [164–498] | 144 [107–153] | 5 (0.42%) |
| LDH previous to IT (U/L) | 235.5 [107–498] | 260 [208–498] | 191 [107–249] | 4 (0.33%) |
| Lymphocytes previous to IT (counts × 10 ⁶ /L) | 1410 [370–2300] | 1580 [370–2300] | 1100 [500–1520] | 2 (0.17%) |
| BRAF | | | | 0 (0%) |
| Wild-type | 10 (83.33%) | 7 (87.5%) | 3 (75%) | |
| Mutated | 2 (16.67%) | 1 (12.5%) | 1 (25%) | |
| No. Previous lines | 0 [0–2] | 0 [0–2] | 0 [0–1] | 0 (0%) |
| Age at start IT | 62.74 [19.1–74.38] | 68.91 [19.1–74.38] | 55.01 [41.32–68.72] | 0 (0%) |
| Toxicity IT | | | | 0 (0%) |
| No | 3 (25%) | 1 (12.5%) | 2 (50%) | |
| Yes | 9 (75%) | 7 (87.5%) | 2 (50%) | |