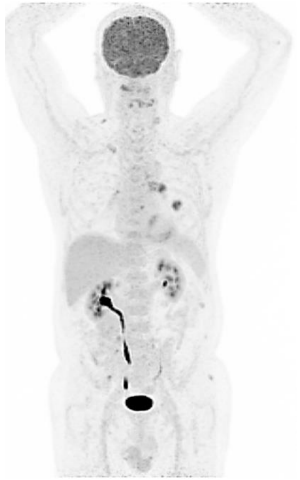


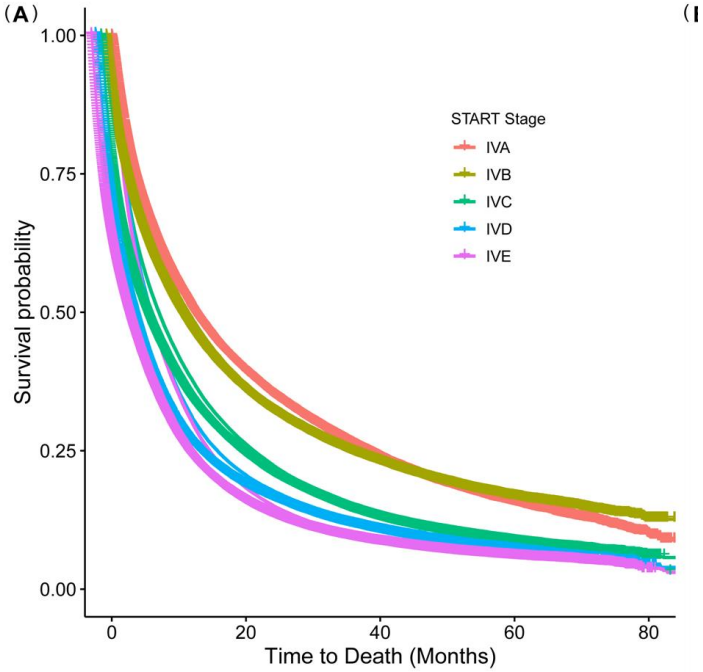
# **Comparaisons des scores cliniques et radiomiques :** prédiction de la survie dans les cancers pulmonaires traités par immunothérapie+/-chimiothérapie

Inserm
La science pour la santé
From science to health

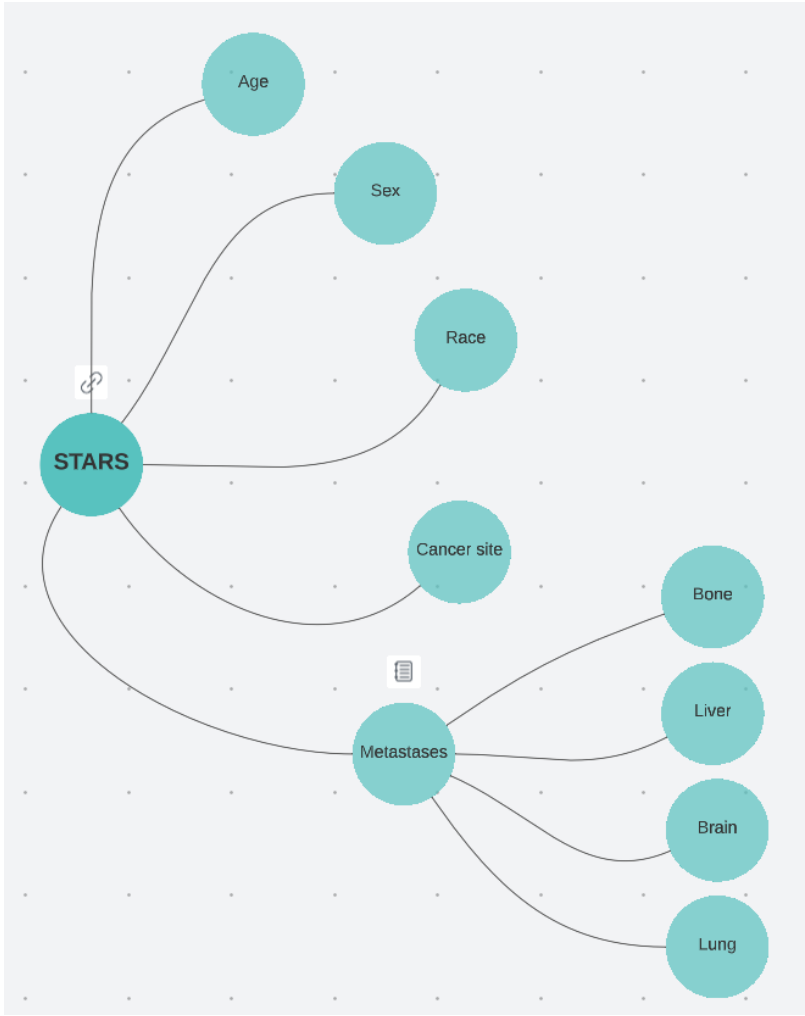
# Scores cliniques issus de la littérature : STARS

https://surv-app.shinyapps.io/phenotype/

*N.G Zaorsky, *et al. Int J Cancer*, 2022.




**Stage IVA**: métastases osseuses (médiane : **12,7 mois**)
**Stage IVB**: métastases pulmonaires (médiane : **11,4 mois**)
**Stage IVC**: métastases pulmonaires/hépatiques (médiane : **7,0 mois**)
**Stage IVD**: metastases pulmonaires/hépatiques/osseuses (médiane : **5,9 mois**)
**Stage IVE**: métastases cérébrales/pulmonaires (médiane : **5,7 mois**)



# Scores cliniques issus de la littérature : STARS

*N.G Zaorsky, *et al. Int J Cancer*, 2022.

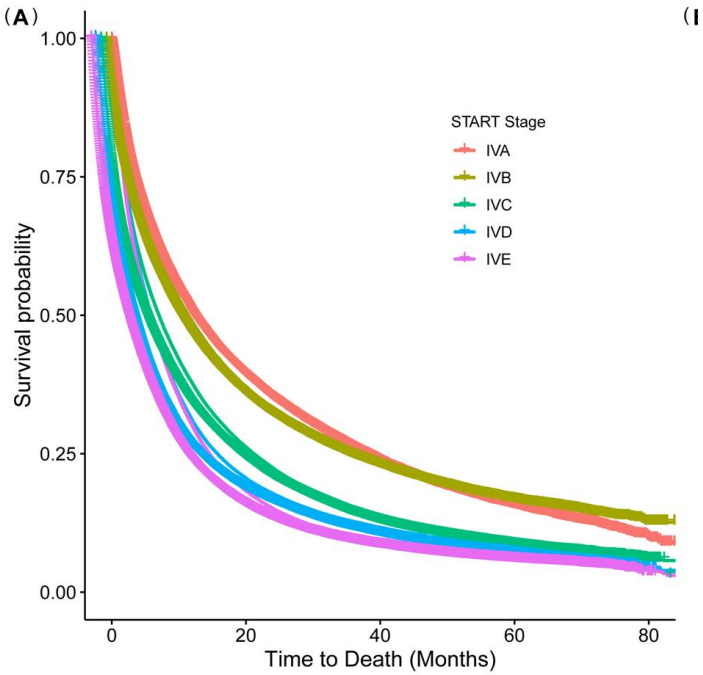



**TABLE 1** Predicted phenotype from latent class analysis and patient characteristics in National Cancer Database (NCDB; 2010-2013)

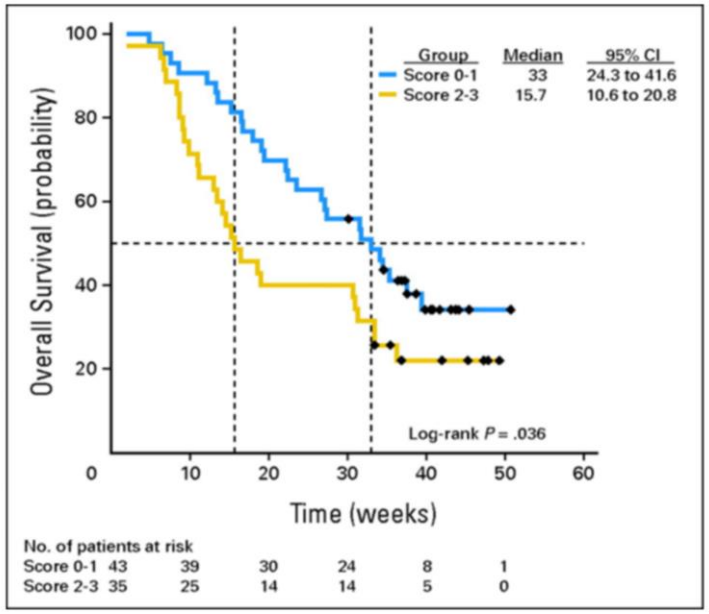
| | | Predicted phenotype | | | | | |
|---|---|---|---|---|---|---|---|
| | All | IVA | IVB | IVC | IVD | IVE | P-value* |
| All | 461 357 | 59 049 (12.80) | 62 491 (13.55) | 130 014 (28.18) | 61 004 (13.22) | 148 799 (32.25) | |
| Cancer site | | | | | | | <.0001 |
| Lung and bronchus | 205 814 (44.61) | 22 747 (38.52) | 0 (0.00) | 3363 (2.59) | 39 142 (64.16) | 140 562 (94.46) | |
| Colorectum | 58 030 (12.58) | 0 (0.00) | 980 (1.57) | 56 483 (43.44) | 234 (0.38) | 333 (0.22) | |
| Pancreas | 50 255 (10.89) | 0 (0.00) | 26 (0.04) | 49 668 (38.20) | 537 (0.88) | 24 (0.02) | |
| Breast | 32 720 (7.09) | 10 438 (17.68) | 8262 (13.22) | 2165 (1.67) | 11 298 (18.52) | 557 (0.37) | |
| Prostate | 19 452 (4.22) | 18 798 (31.83) | 215 (0.34) | 224 (0.17) | 150 (0.25) | 65 (0.04) | |
| Stomach | 16 943 (3.67) | 715 (1.21) | 8066 (12.91) | 7780 (5.98) | 382 (0.63) | 0 (0.00) | |
| Kidney | 16 850 (3.65) | 2700 (4.57) | 8837 (14.14) | 153 (0.12) | 4050 (6.64) | 1110 (0.75) | |
| Ovary | 10 657 (2.31) | 0 (0.00) | 8600 (13.76) | 2057 (1.58) | 0 (0.00) | 0 (0.00) | |
| Esophagus | 12 112 (2.63) | 558 (0.94) | 4131 (6.61) | 4523 (3.48) | 2430 (3.98) | 470 (0.32) | |
| Uterus | 8064 (1.75) | 0 (0.00) | 7813 (12.50) | 0 (0.00) | 251 (0.41) | 0 (0.00) | |
| Liver | 6391 (1.39) | 1493 (2.53) | 4772 (7.64) | 0 (0.00) | 126 (0.21) | 0 (0.00) | |
| Melanoma | 6244 (1.35) | 0 (0.00) | 7 (0.01) | 0 (0.00) | 652 (1.07) | 5585 (3.75) | |
| Gallbladder | 3090 (0.67) | 23 (0.04) | 0 (0.00) | 3050 (2.35) | 4 (0.01) | 13 (0.01) | |
| Bladder | 5190 (1.12) | 1195 (2.02) | 2723 (4.36) | 548 (0.42) | 644 (1.06) | 80 (0.05) | |
| Soft tissue | 3586 (0.78) | 2 (0.00) | 2800 (4.48) | 0 (0.00) | 784 (1.29) | 0 (0.00) | |
| Cervix | 3648 (0.79) | 0 (0.00) | 3440 (5.50) | 0 (0.00) | 208 (0.34) | 0 (0.00) | |
| Thyroid | 2311 (0.50) | 380 (0.64) | 1819 (2.91) | 0 (0.00) | 112 (0.18) | 0 (0.00) | |

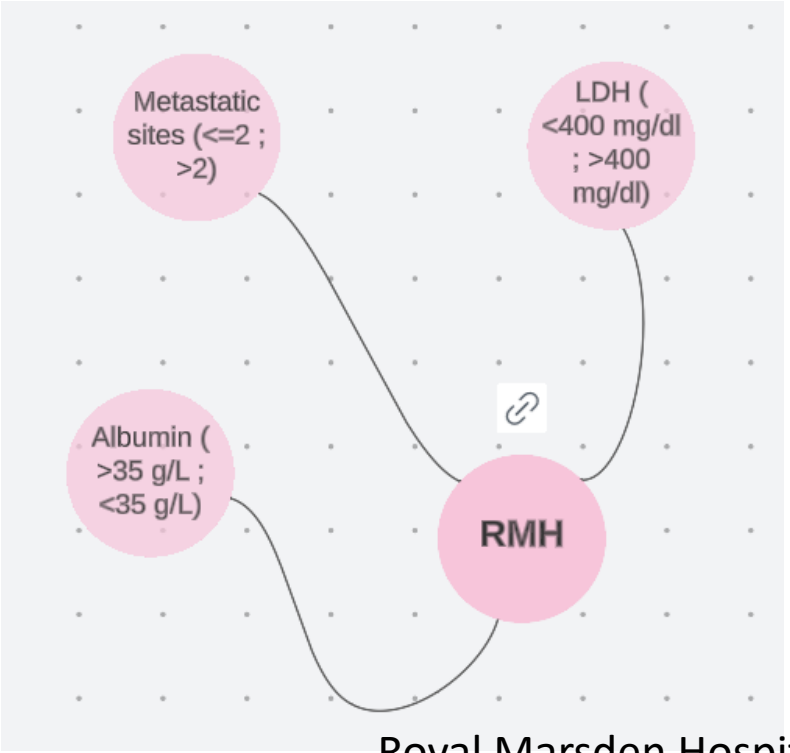
**Stage IVA**: métastases osseuses (médiane : **12,7 mois**)
**Stage IVB**: métastases pulmonaires (médiane : **11,4 mois**)
**Stage IVC**: métastases pulmonaires/hépatiques (médiane : **7,0 mois**)
**Stage IVD**: metastases pulmonaires/hépatiques/osseuses (médiane : **5,9 mois**)
**Stage IVE**: métastases cérébrales/pulmonaires (médiane : **5,7 mois**)

→ "STARS is the first system that takes a **pan-cancer approach to metastatic cancer staging**."

# Scores cliniques issus de la littérature : RMH

*H.T Arkeneau, *et al. J Clin Oncol*, 2009.




Royal Marsden Hospital Score

- n = 78 patients
- Cancers localement avancés/métastasiques : gastrointestinal (39%), sein/gynécologique (24%), sarcomes (10%), thoracique/tête et cou (8%)…
- Métastases : poumon (55%), foie (45%), os (10%)…
- Traitements :

# Scores cliniques issus de la littérature : RMH

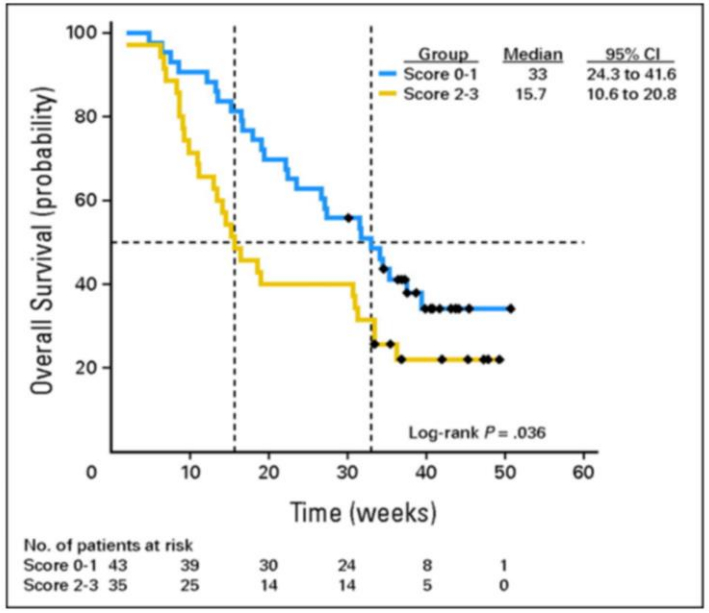



**Table 4.** Overall Survival According to Prognostic Score (n = 78)

| Variable | Overall Survival (weeks) Median | 95% CI | Univariate Log-Rank *P* | HR | 95% CI | Multivariate Cox Regression *P* |
|---|---|---|---|---|---|---|
| Prognostic score | | | < .036 | 1.4 | 1.02 to 1.88 | .036 |
| 0-1 | 33.0 | 24 to 42 | | | | |
| 2-3 | 15.7 | 11 to 21 | | | | |
| WBC count | | | < .003 | 0.40 | 0.20 to .80 | .009 |
| > 10,500/μL | 15.7 | 12 to 19 | | | | |
| Normal | 31.6 | 26 to 38 | | | | |
| Hemoglobin | | | .05 | 1.16 | 0.64 to 2.09 | .633 |
| < 12 g/dL | 15.7 | 8 to 23 | | | | |
| Normal | 33.4 | 30 to 37 | | | | |

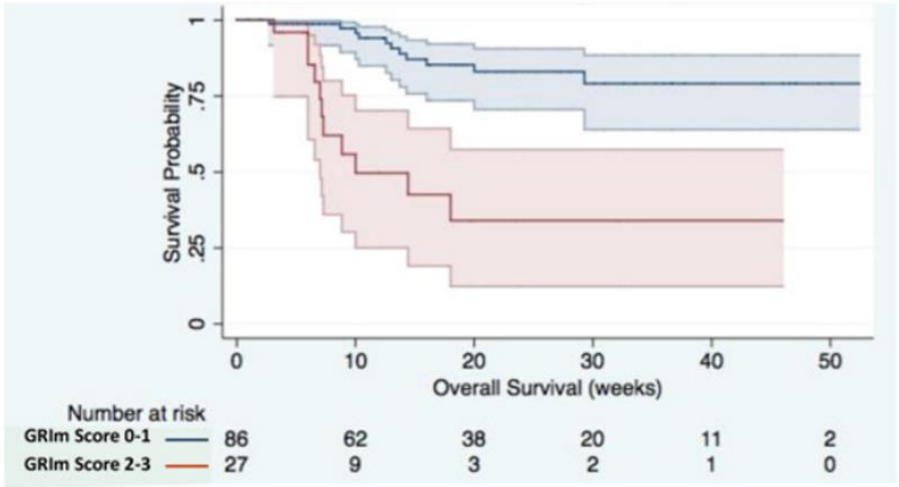
Abbreviation: HR, hazard ratio.

- n = 78 patients
- Cancers localement avancés/métastasiques : gastrointestinal (39%), sein/gynécologique (24%), sarcomes (10%), thoracique/tête et cou (8%)…
- Métastases : poumon (55%), foie (45%), os (10%)…
- Traitements : agents biologiques (68%), agents cytotoxiques (32%)

→ "This is the first **prospective** analysis confirming that a prognostic score based on objective markers, including **albumin** less than 35 g/L, **LDH** more than ULN, and more than two **sites of metastasis**, is a **helpful tool in the process of patient selection for phase I trial entry**".

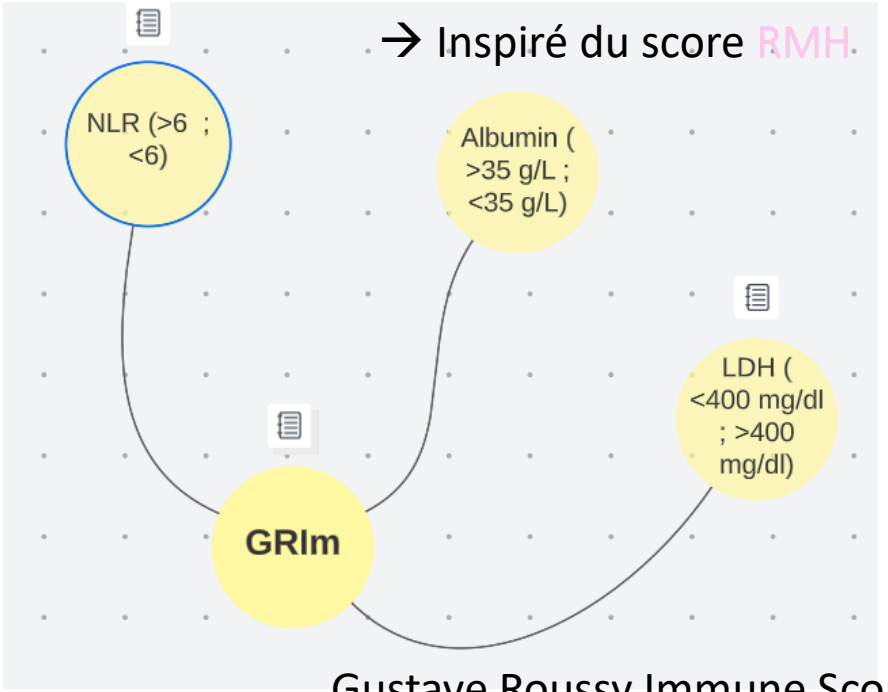
# Scores cliniques issus de la littérature : GRIm

*F. Bigot, *et al. Eur J Cancer*, 2017.




| Risk according to the GRIm-Score | OS (m) | 95% CI | HR (95% CI) | Harrell C-index |
|---|---|---|---|---|
| High risk (2–3) | 4 | 1.93–6.1 | 2.94 (1.87–4.64) | 0.7 |
| Low risk (0–1) | 17 | 13.76–20.24 | | |

- n = 155 patients
- Cancers localement avancés/métastasiques : NSCLC (19,3%), tête et cou (11,6%), urothéliale (10,3%), rénal (9%), sein (7,7%), utérus (6,4%)…
- Traitements: immunothérapie seule ou associative




Gustave Roussy Immune Score

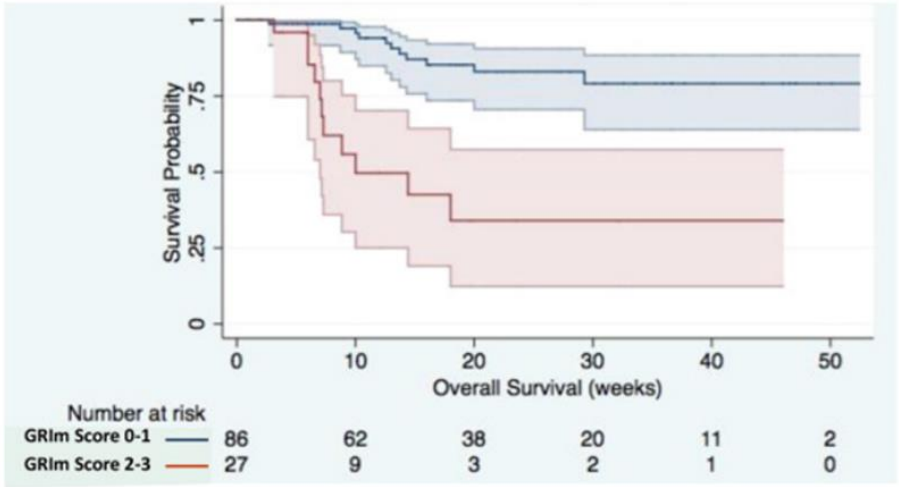
Table 2
Repartition of ICT trials in the validation cohort.

| ICT trials | N | % |
|---|---|---|
| Anti-PD1 | 64 | 41.3 |
| Anti-PD-L1 | 64 | 41.3 |
| Anti-GITR | 23 | 14.8 |
| Anti-PD-L1 + anti-CSF1R | 2 | 1.3 |
| Anti-PD1 + anti-CD137 | 2 | 1.3 |
| Total | 155 | 100 |

PD1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1; GITR, glucocorticoid-induced tumour necrosis factor receptor; CSF1R, Colony stimulating factor 1 receptor; CD137, cluster of differentiation 137; ICT, immune-checkpoint therapy.

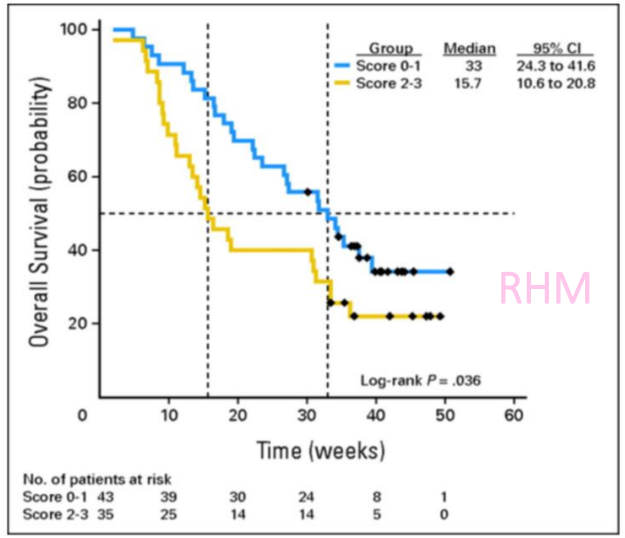
# Scores cliniques issus de la littérature : GRIm

*F. Bigot, *et al. Eur J Cancer*, 2017.




| Risk according to the GRIm-Score | OS (m) | 95% CI | HR (95% CI) | Harrell C-index |
|---|---|---|---|---|
| High risk (2–3) | 4 | 1.93–6.1 | 2.94 (1.87–4.64) | 0.7 |
| Low risk (0–1) | 17 | 13.76–20.24 | | |

*H.T Arkeneau, *et al. J Clin Oncol*, 2009.



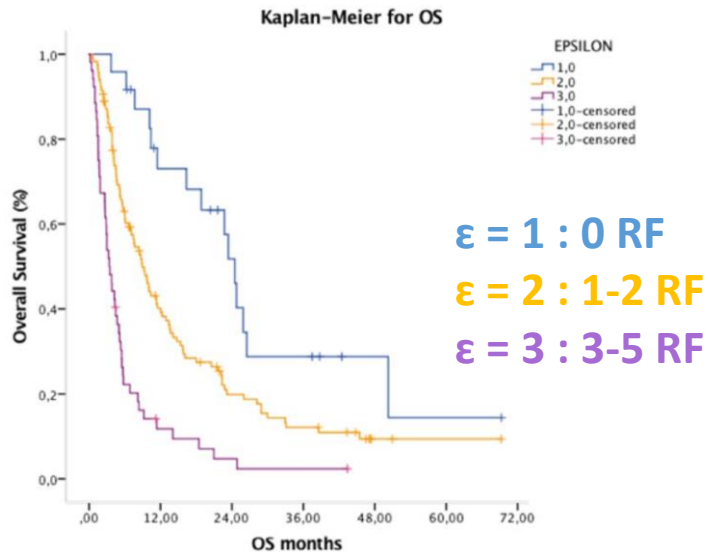

RHM

→ "The Gustave Roussy Immune Score, based on **albumin**, **LDH** and **NLR**, allows a **better selection of patients for ICT phase I trials**".

- n = 155 patients
- Cancers localement avancés/métastasiques : NSCLC (19,3%), tête et cou (11,6%), urothéliale (10,3%), rénal (9%), sein (7,7%), utérus (6,4%)…
- Traitements: immunothérapie seule ou associative

# Scores cliniques issus de la littérature : EPSILoN

*A. Prelaj, *et al. Cancers*, 2019.

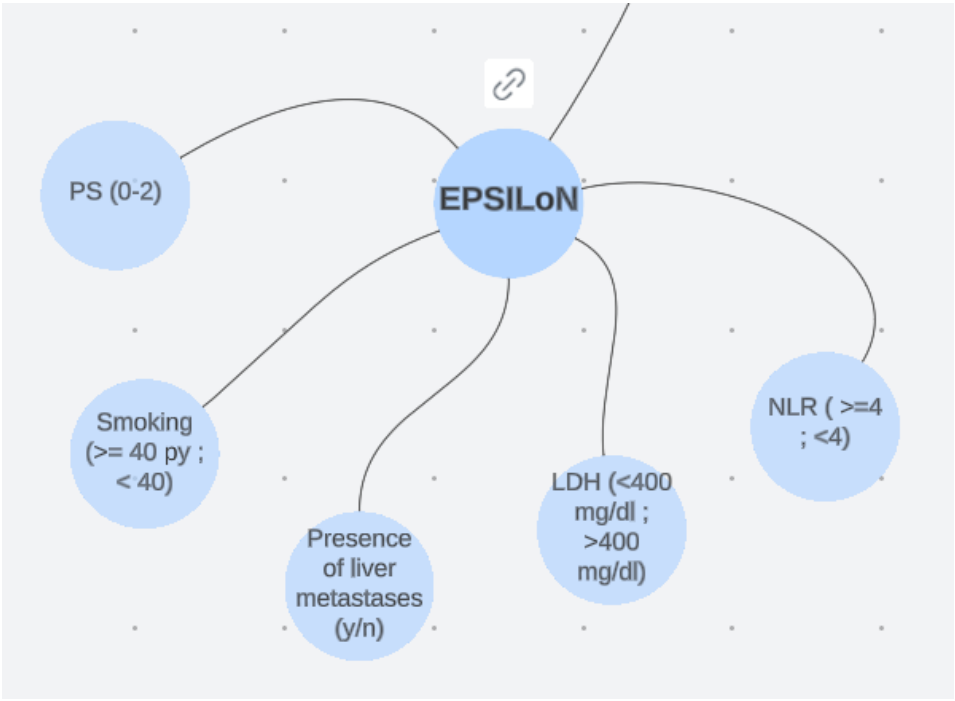



ε = 1 : 0 RF

ε = 2 : 1-2 RF

ε = 3 : 3-5 RF

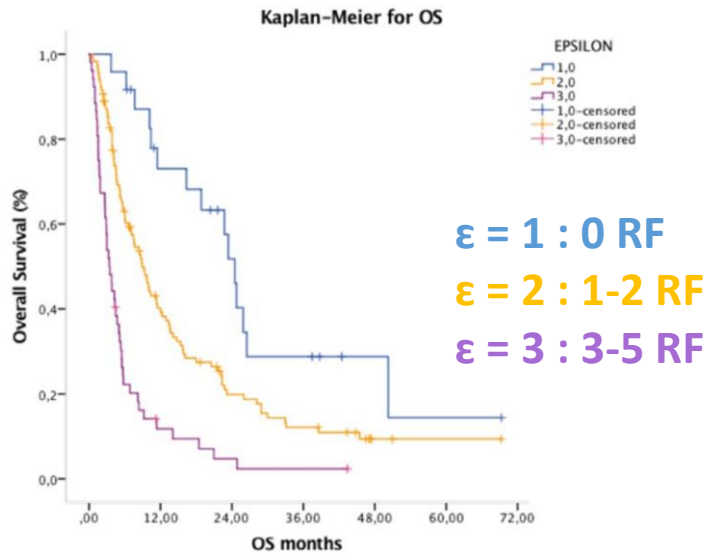
Median OS of the three prognostic groups were 24.5, 8.9 and 3.4 months, respectively (HR 2.40, 95% CI 1.82–3.17, p < 0.001).




- n = 193 patients NSCLC (stades IIIb–c et IV)
- Traitements: anti-PD 1 ou anti PD-L1 (2ème ou 3ème ligne)

# Scores cliniques issus de la littérature : EPSILoN

*A. Prelaj, *et al. Cancers*, 2019.




ε = 1 : 0 RF

ε = 2 : 1-2 RF

ε = 3 : 3-5 RF

Median OS of the three prognostic groups were 24.5, 8.9 and 3.4 months, respectively (HR 2.40, 95% CI 1.82–3.17, p < 0.001).

- n = 193 patients NSCLC (stades IIIb–c et IV)
- Traitements: anti-PD 1 ou anti PD-L1 (2ème ou 3ème ligne)

**Table 3.** Baseline predictive score: EPSILoN (ECOG PS, smoking, liver metastases, LDH, NLR; ε score).

| Prognostic Factor | Assessment | Point |
|---|---|---|
| ECOG PS | 1 | 0 |
| | 2 | 1 |
| Smoking (pack years) | ≥40 | 0 |
| | <40 | 1 |
| Liver metastases | No | 0 |
| | Yes | 1 |
| LDH (mg/dL) | <400 | 0 |
| | ≥400 | 1 |
| NLR | <4 | 0 |
| | ≥4 | 1 |
| **Prognostic groups** (points): best = 0; intermediate = 1–2; poor = 3–5 | | |

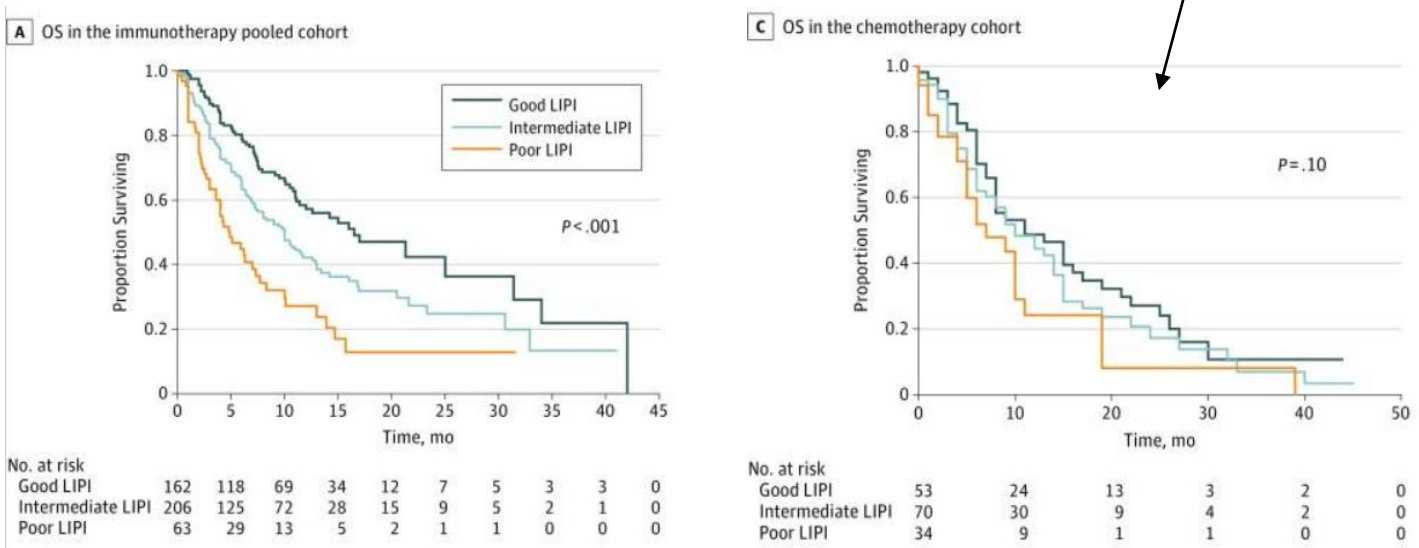
ECOG, Eastern Cooperative Oncology Group; PS, performance status; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio.

→ "This score statistically significantly identifies **three different prognostic groups** of patients and could be a **useful tool to guide treatment decisions"**.

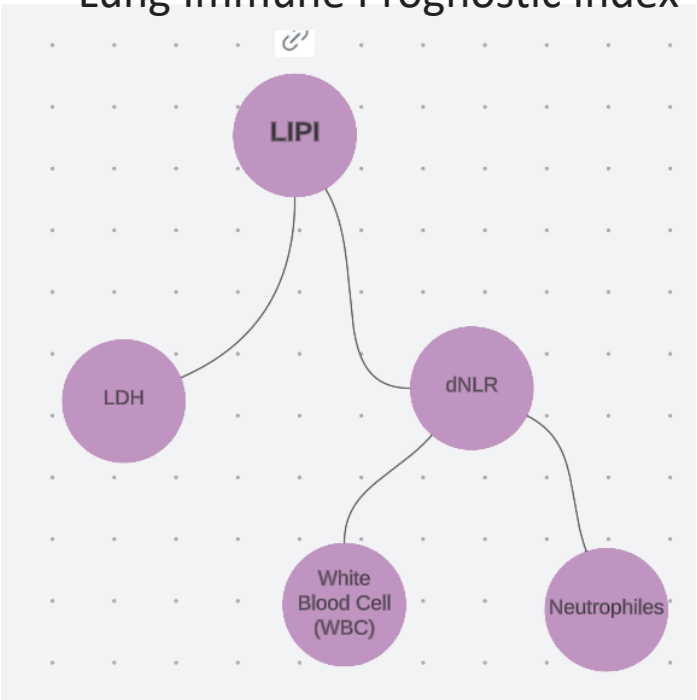
# Scores cliniques issus de la littérature : LIPI

*L. Mezquita, *et al. JAMA Oncol*, 2018.

Contrôle : n = 161




Lung Immune Prognostic Index




- n = 161 patients NSCLC (test set) , n = 305 patients NSCLC (validation test)
- Traitements: anti-PD 1 ou anti PD-L1

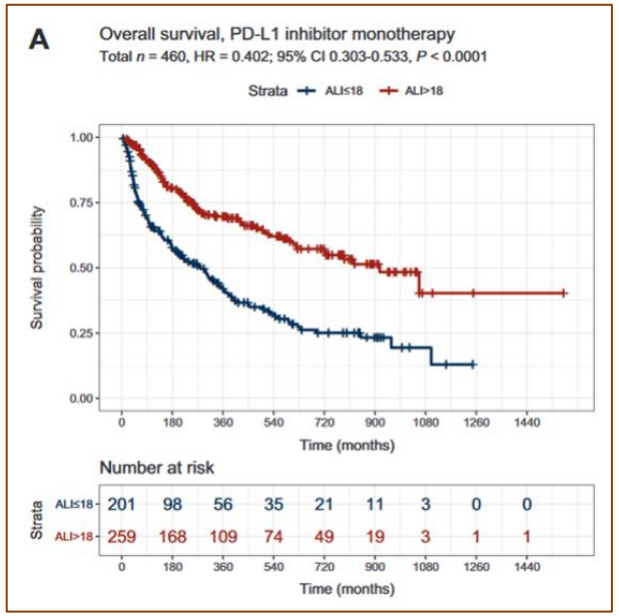
→ “Poor baseline LIPI, combining **dNLR greater than 3 and LDH greater than ULN**, was correlated with **poor outcomes with immunotherapy**, but not chemotherapy, raising the hypothesis that **LIPI** might be useful for **identifying patients unlikely to benefit from treatment**”.

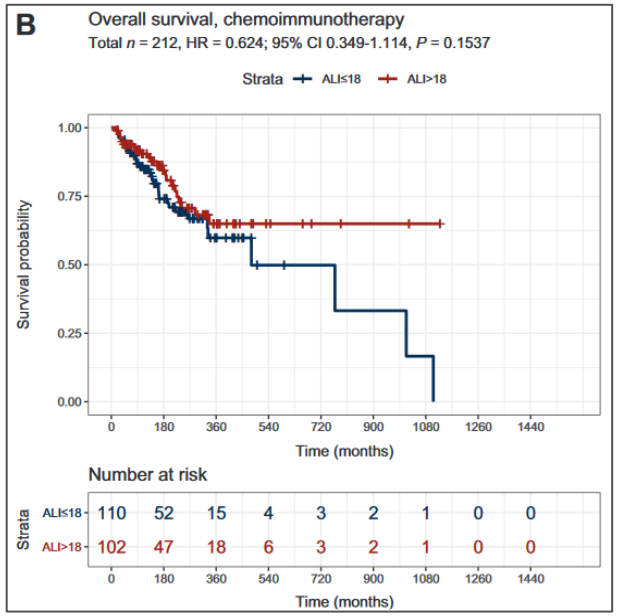
# Prédiction de la survie : ALI

ALI = (BMI*Albumin)/ NLR

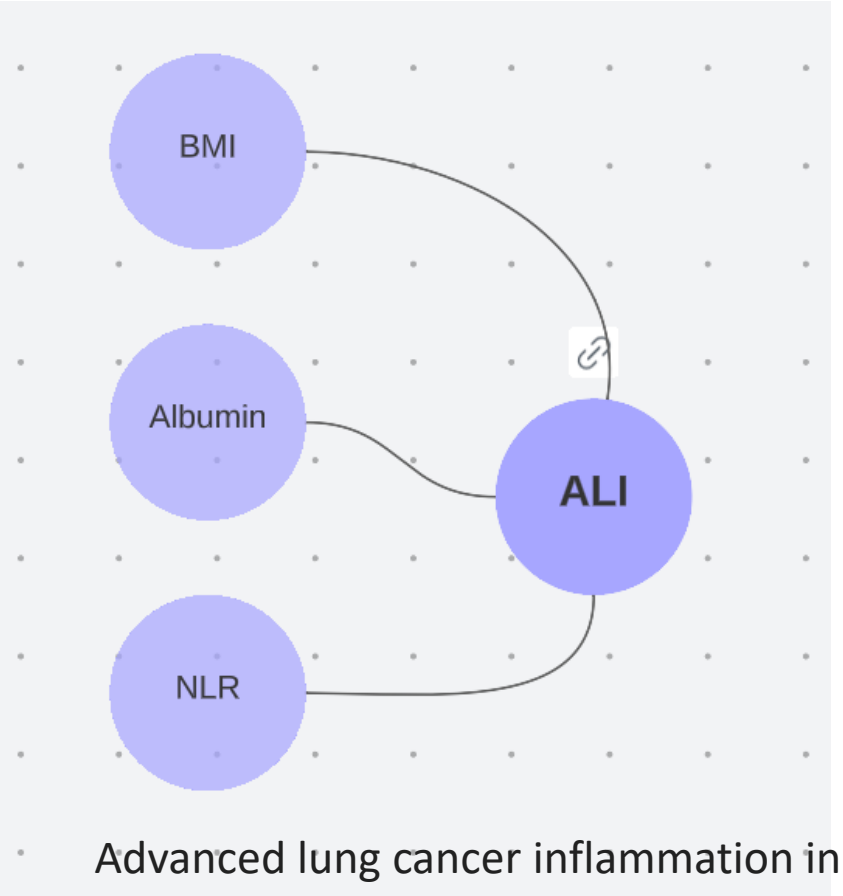
ALI = reflet de l'inflammation systémique et du phénomène de cachexie.

*G. Mountzios, *et al. ESMO open*, 2021.




→ **Biomarqueur pour l'efficacité de l'immunothérapie ?**

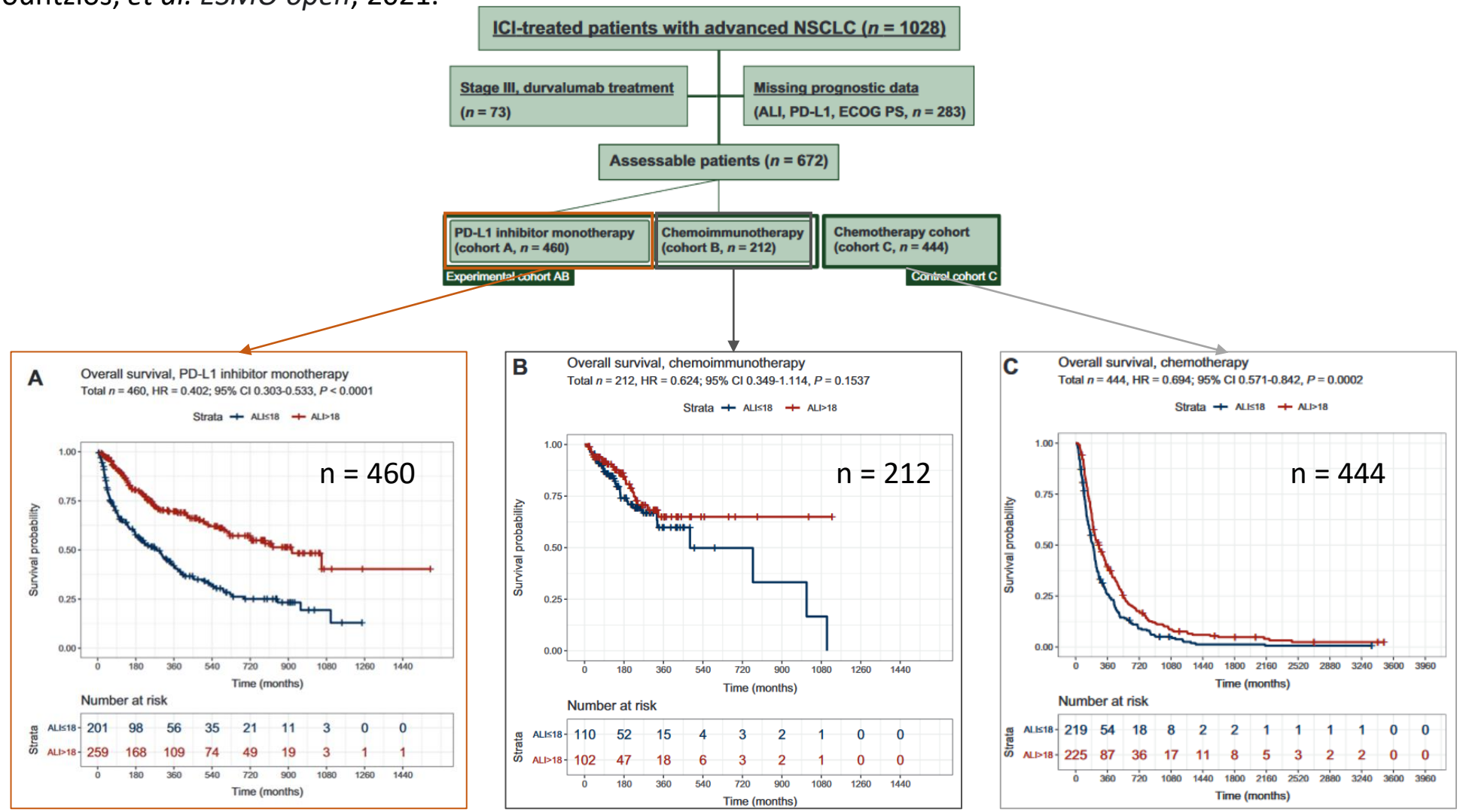



Advanced lung cancer inflammation index

ALI = (BMI*Albumin)/ NLR

# Prédiction de la survie : ALI

*G. Mountzios, *et al. ESMO open*, 2021.

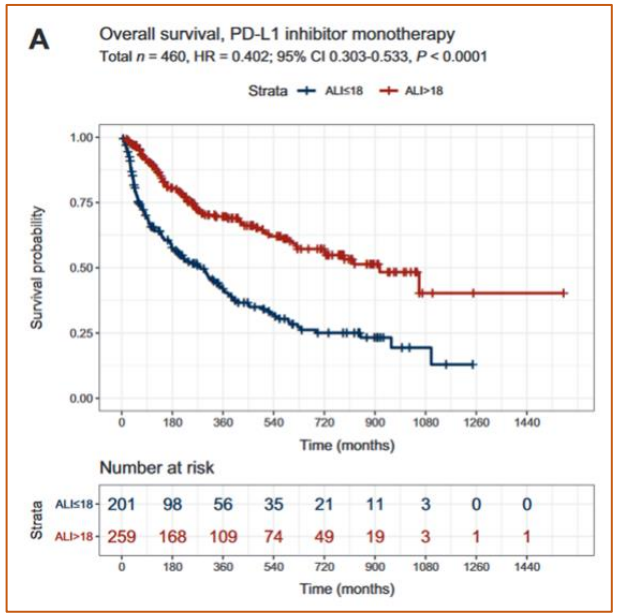


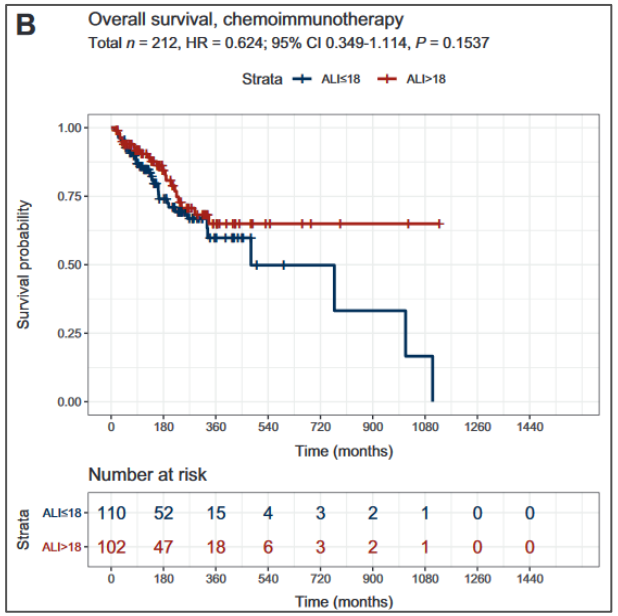
ALI = (BMI*Albumin)/ NLR

# Prédiction de la survie : ALI

*G. Mountzios, *et al. ESMO open*, 2021.

Cutoff bibliographie




| | cohort A (IO-monotherapy, n=460) | | cohort B (chemoimmunotherapy, n=212) | |
|---|---|---|---|---|
| | HR (95% CI) | P-value | HR (95% CI) | P-value |
| age | 1.00 (0.99-1.02) | 0.82 | 1.03 (0.99-1.04) | 0.28 |
| sex | 0.99 (0.74-1.33_ | 0.97 | 1.68 (0.93-3.02) | 0.08 |
| ALI > 18 | 0.41 (0.31-0.54) | <0.0001 | 0.68 (0.40-1.16) | 0.16 |
| NLR < 5 | 0.48 (0.37-0.63) | <0.0001 | 0.88 (0.52-1.49) | 0.63 |
| PD-L1 TPS 1-49 | 0.91 (0.64-1.30) | 0.61 | 1.14 (0.59-2.20) | 0.70 |
| PD-L1 TPS ≥ 50 | 0.52 (0.36-0.75) | <0.0001 | 0.93 (0.43-2.02) | 0.86 |
| ECOG PS =1 | 2.30 (1.64-3.22) | <0.0001 | 2.24 (1.10-4.56) | 0.026 |
| ECOG PS >1 | 4.12 (2.72-6.24) | <0.0001 | 9.50 (4.45-20.25) | <0.0001 |
| Line (first *vs.* later) | 1.43 (1.23-1.68) | <0.0001 | --- | |
| BMI >25 | 0.69 (0.52-0.91) | 0.008 | 0.65 (0.67-1.92) | 0.65 |
| Weight >72 | 0.69 (0.52-0.90) | 0.007 | 1.35 (0.79-2.31) | 0.27 |
| Height >1.70 | 1.12 (0.86-1.47) | 0.41 | 1.65 (0.96-2.83) | 0.07 |
| Albumin >3.9 | 0.46 (0.34-0.62) | <0.0001 | 0.40 (0.23-0.69) | 0.001 [1] |

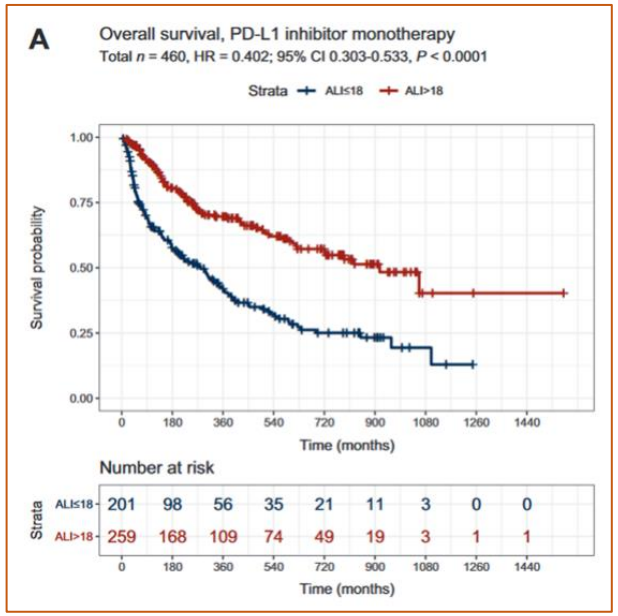
Cutoff par la médiane

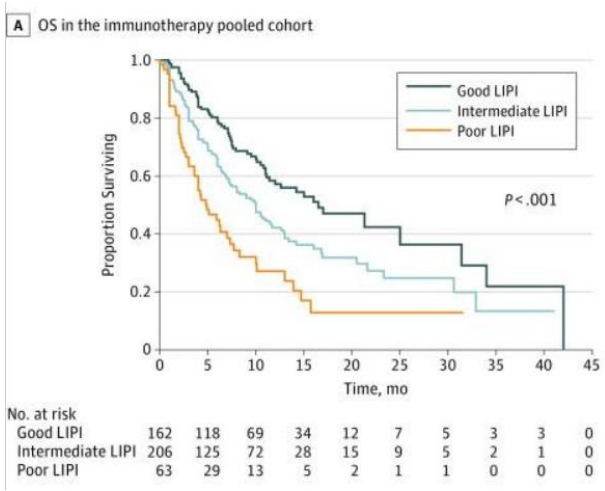
→ “The ALI score is a powerful prognostic and predictive **biomarker for patients with advanced NSCLC treated with PD-L1 inhibitors alone**, but not in combination with chemotherapy”.

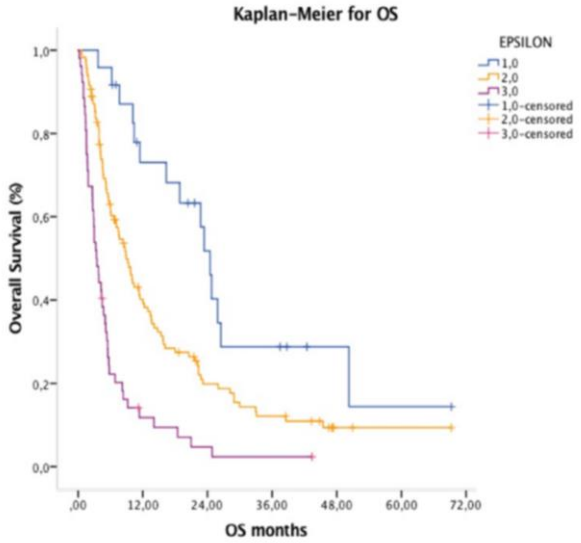
ALI = (BMI*Albumin)/ NLR

# Prédiction de la survie : ALI

*G. Mountzios, *et al. ESMO open*, 2021.




| | cohort A (IO-monotherapy, n=206) | | cohort B (chemoimmunotherapy, n=107) | |
|---|---|---|---|---|
| | OS HR (95% CI) | p-value | OS HR (95% CI) | p-value |
| ALI > 18 | 0.45 (0.30-0.65) | <0.0001 | 1.51 (0.63-3.65) | 0.36 |
| dNLR < 3 | 0.59 (0.42-0.84) | 0.004 | 2.51 (1.06-5.92) | 0.036 |
| LDH < 248 (median) | 0.53 (0.37-0.76) | 0.0005 | 0.40 (0.18-0.93) | 0.034 |
| LIPI low | 0.57 (0.45-0.73) | <0.0001 | 0.79 (0.34-1.83) | 0.58 |
| EPSILoN low | 0.43 (0.30-0.61) | <0.0001 | 0.59 (0.22-1.59) | 0.30 |

→ “Its association with outcomes is **stronger than that of other parameters** (PD-L1 TPS, NLR, lung immune prognostic index, EPSILoN)”.

# Bases de données : TIPIT & Capricorne

- n = 100 patients NSCLC stade IV
- TEP/TDM au 18F FDG préthérapeutique
- Données cliniques, biologiques, radiomiques
- Traitement par **chimio-immunothérapie**

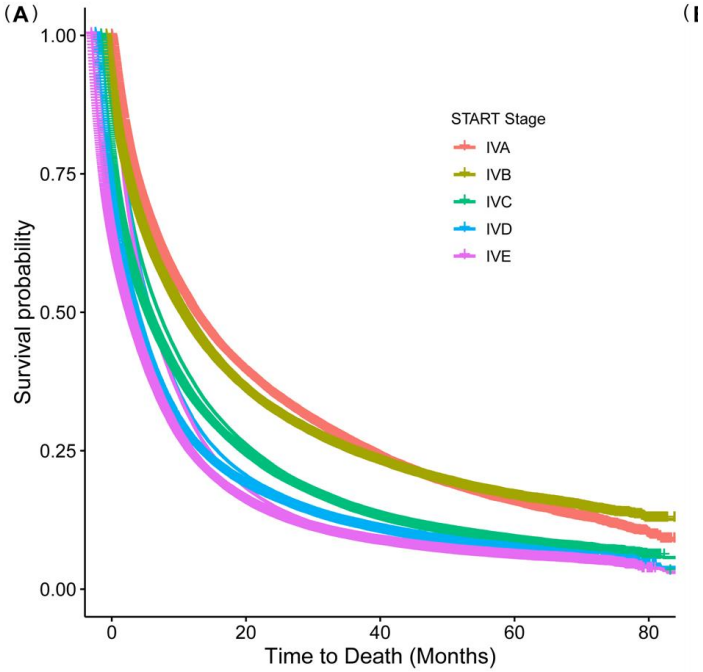
| | Cutoff | p (log-rank) |
|---|---|---|
| **Age (y)** | **75** | **0.004** |
| Sex | / | 0.85 |
| BMI (kg/m²) | 26.037 | 0.066 |
| PS | / | 0.37 |
| **Lymphocytes (10^9/L)** | **1.85** | **0.025** |
| **Neutrophiles (10^9/L)** | **5.91** | **0.024** |
| NLR | 4.44 | 0.059 |
| **Albumine (g/L)** | **40.1** | **0.015** |
| LDH (U/L) | 248 U/L | 0.41 |
| PDL1 (%) | 60 | 0.23 |
| **TMTV (mL)** | **52.51** | **0.004** |
| Dmax (vx) | 32.3 | 0.2 |
| Bone (mL) | 1.90 | 0.12 |
| **Lung (mL)** | **21.71** | **0.023** |
| **Sub_Nodes** | **0.74** | **0.034** |
| **Supra_Nodes** | **26.872** | **0.007** |

- n = 74 patients NSCLC stade IV
- TEP/TDM au 18F FDG préthérapeutique
- Données cliniques, biologiques, radiomiques
- Traitement par **immunothérapie (anti PD 1)**

| | Cutoff | p (log-rank) |
|---|---|---|
| Age (y) | 60 | 0.005 |
| **Sex** | **/** | **0.046** |
| BMI (kg/m²) | 26.24 | 0.14 |
| PS | / | 0.22 |
| **Lymphocytes (10^9/L)** | **1.84** | **0.021** |
| Neutrophiles (10^9/L) | 7.52 | 0.053 |
| **Leucocytes (10^9/L)** | **9.48** | **0.017** |
| **NLR** | **4.78** | **0.006** |
| dNLR | 2.59 | 0.27 |
| **Albumine (g/L)** | **40** | **0.01** |
| **LDH (U/L)** | **194** | **0.05** |
| PDL1 (%) | 80 | 0.16 |
| **TMTV (mL)** | **90** | **0.017** |
| **Dmax (vx)** | **28.4** | **0.001** |
| **Bone (mL)** | **8.57** | **0.022** |
| **Lung (mL)** | **66.79** | **0.033** |
| Sub_Nodes | 0.54 | 0.12 |
| Supra_Nodes | 46.98 | 0.11 |

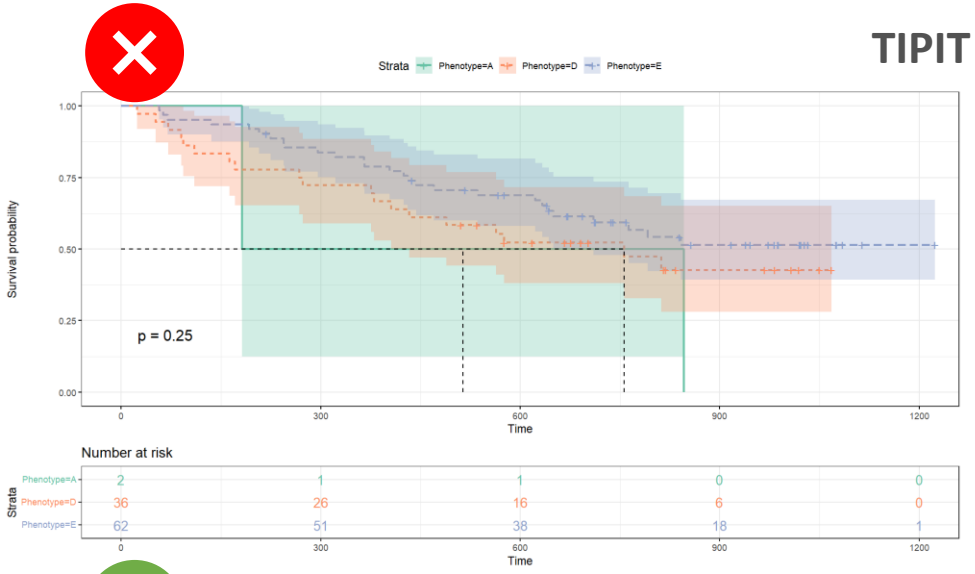
# Prédiction de la survie : STARS

*N.G Zaorsky, *et al. Int J Cancer*, 2022.

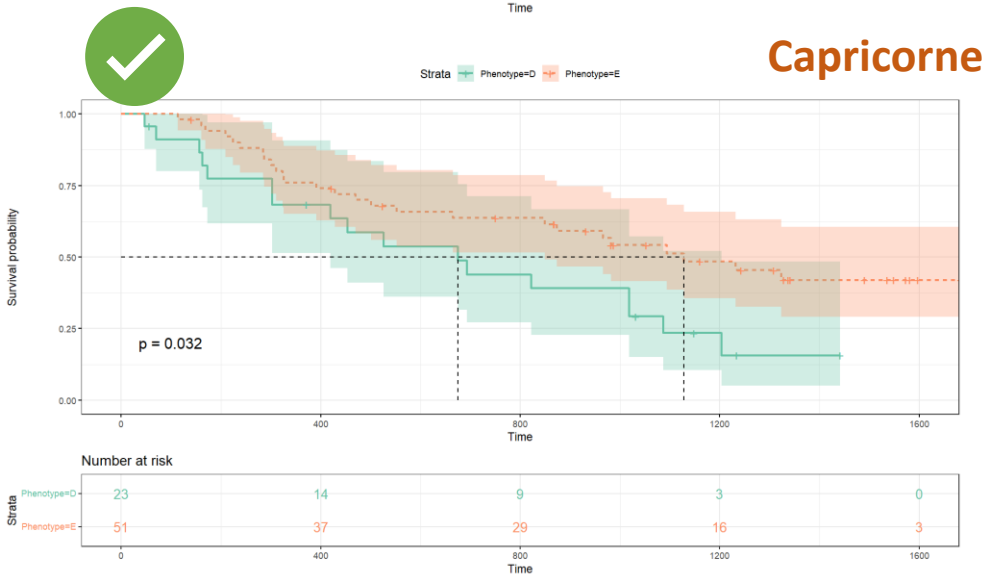



Stage IVA: métastases osseuses
Stage IVB: métastases pulmonaires
Stage IVC: métastases pulmonaires/hépatiques
Stage IVD: metastases pulmonaires/hépatiques/osseuses
Stage IVE: métastases cérébrales/pulmonaires

**TIPIT**



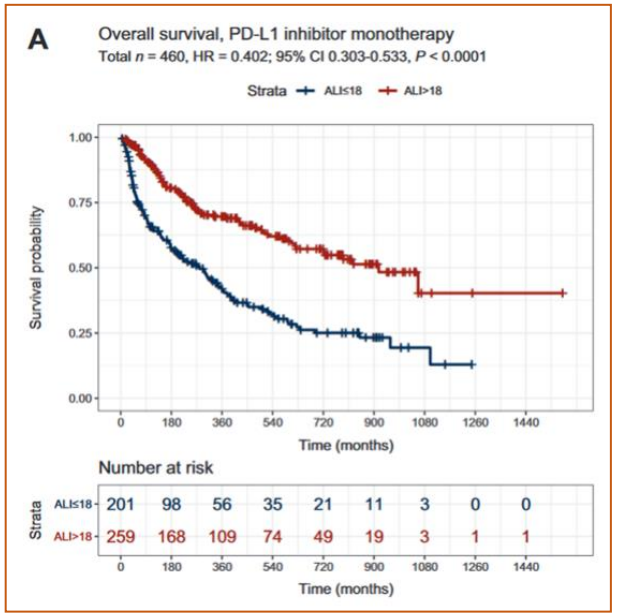

**Capricorne**

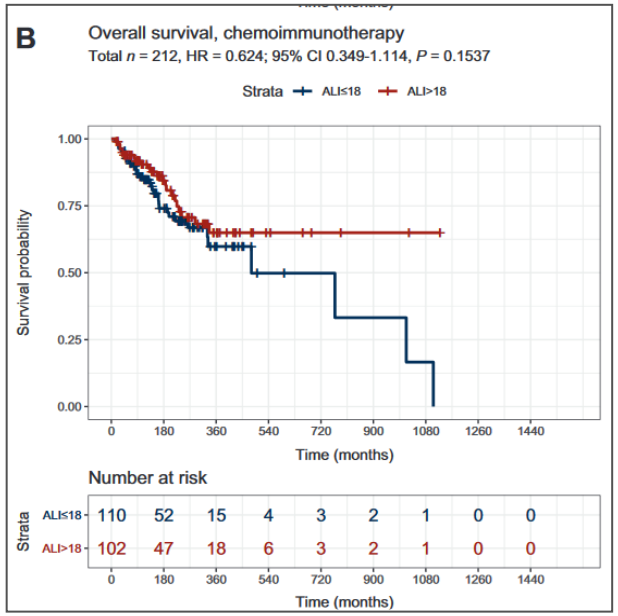


# Prédiction de la survie : ALI

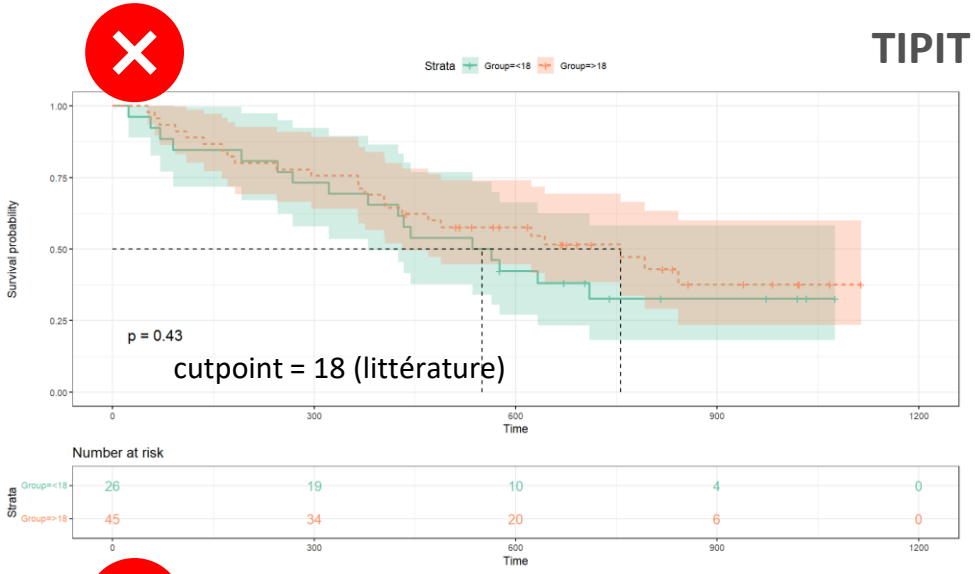
ALI = (BMI*Albumin)/ NLR

*G Mountzios, *et al. ESMO Open,* 2021.

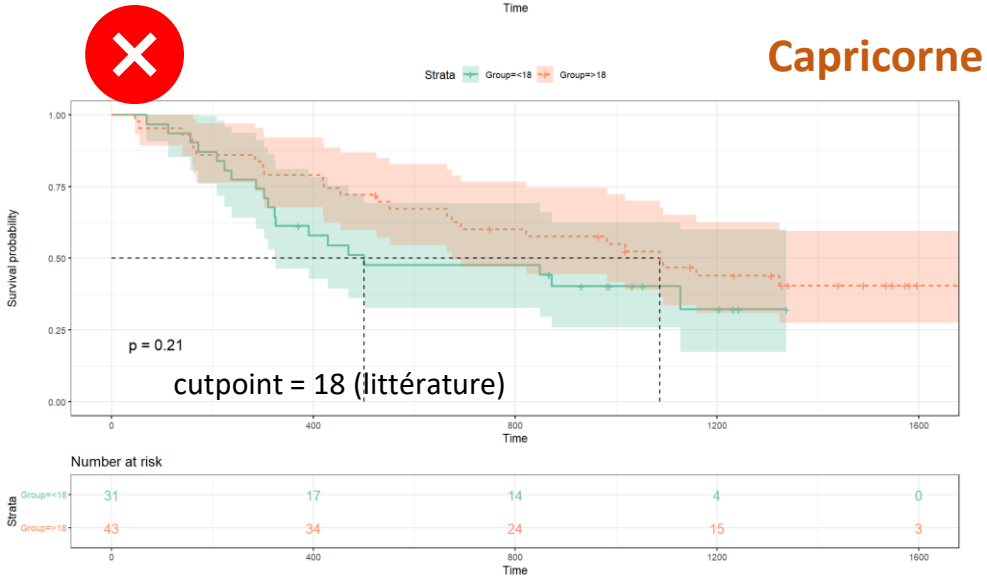



**TIPIT**



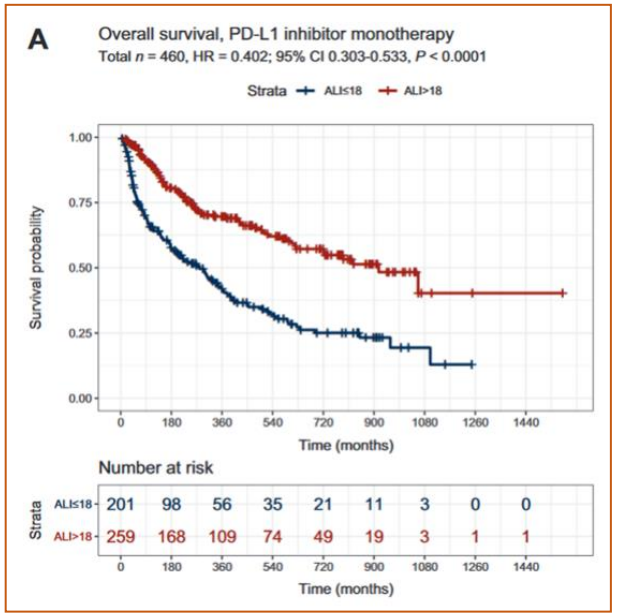

**Capricorne**

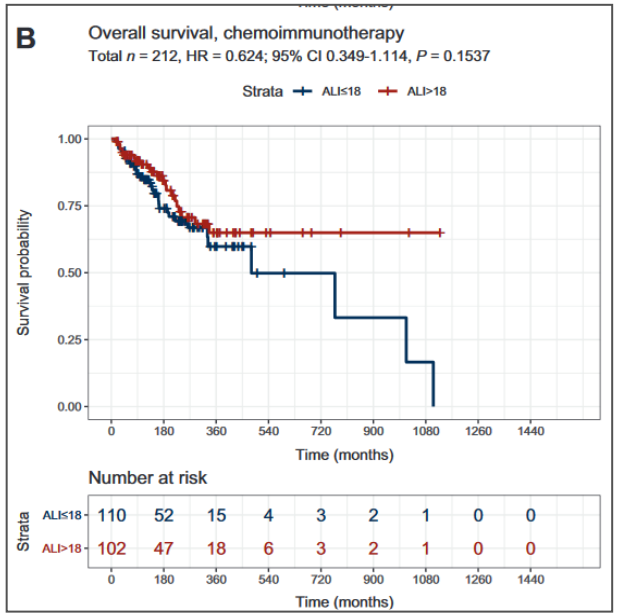


# Prédiction de la survie : ALI

ALI = (BMI*Albumin)/ NLR

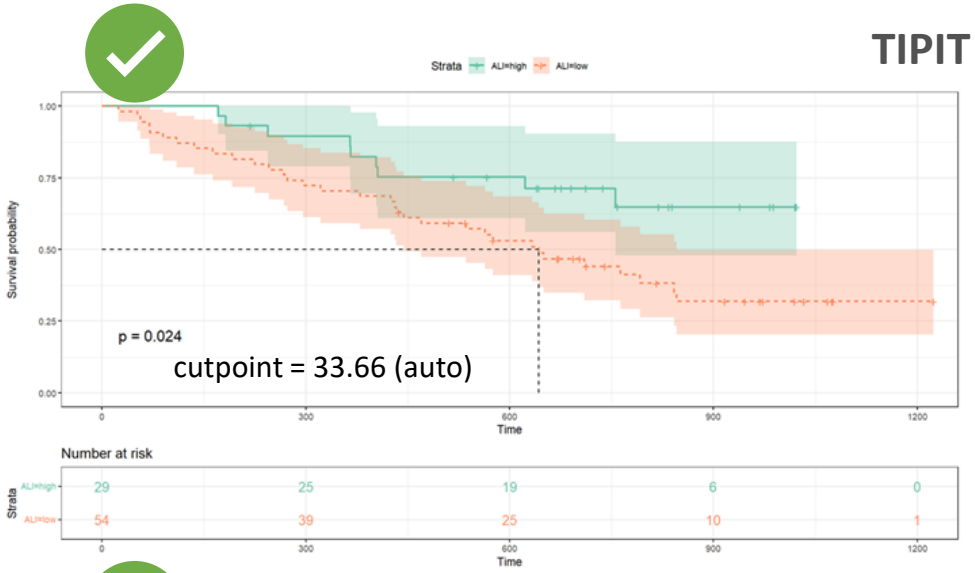
*G Mountzios, *et al. ESMO Open,* 2021.



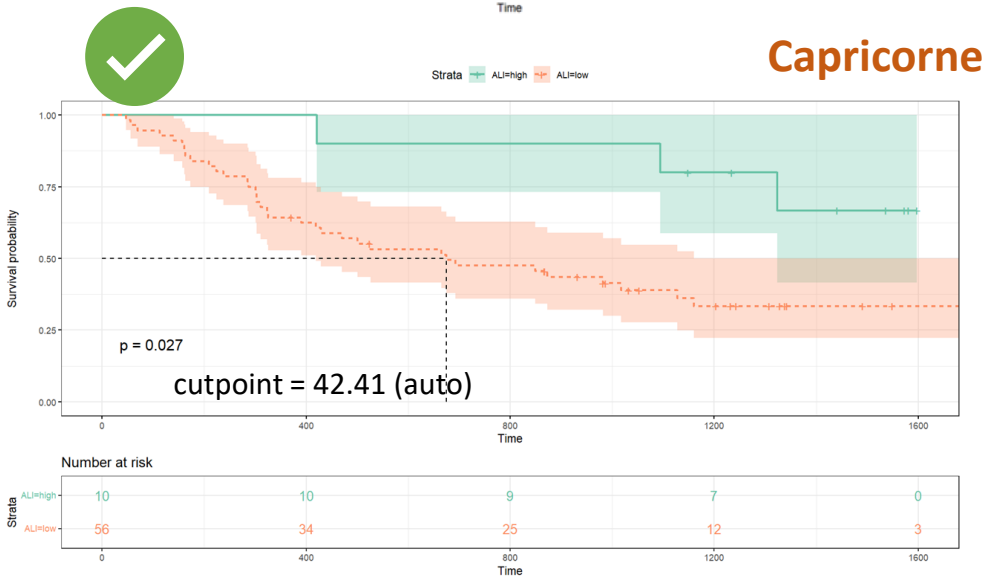




**Peut-on améliorer la prédiction de la survie globale par la combinaison de scores cliniques et radiomiques ?**

**TIPIT**

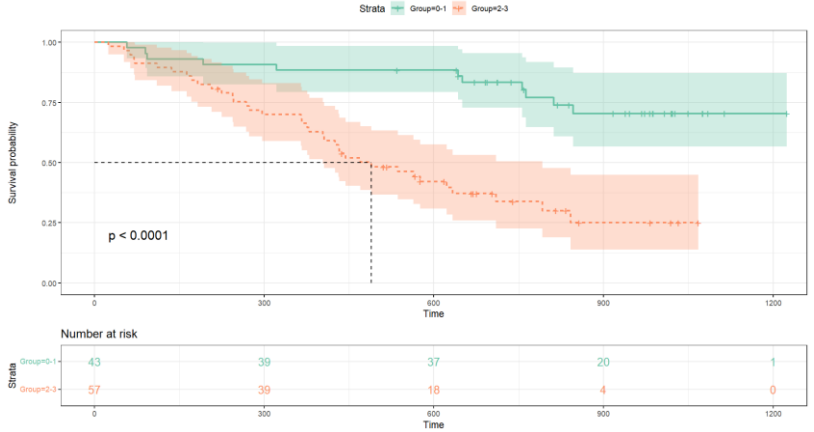



**Capricorne**

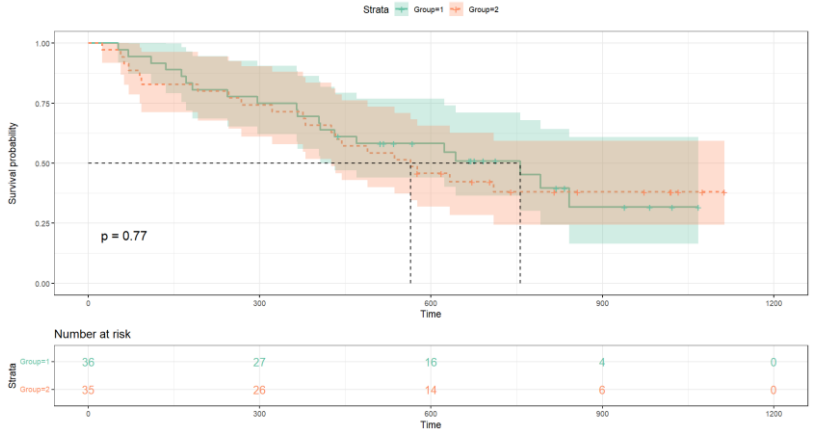


# Comparaisons des modèles: TIPIT

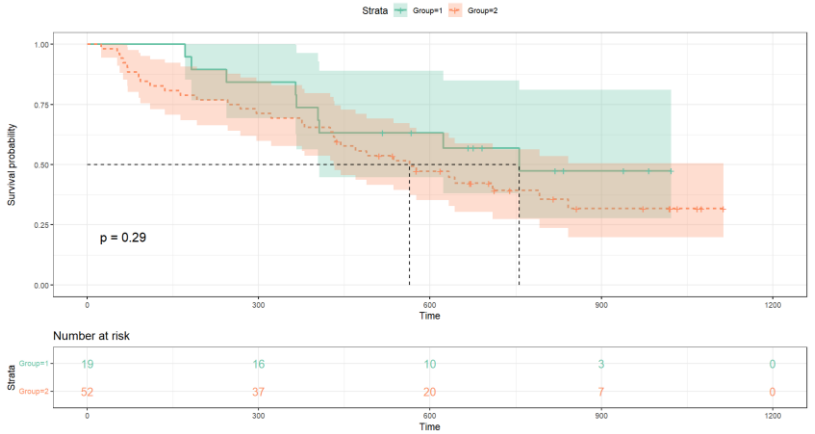
## TMTV + BMI + Age



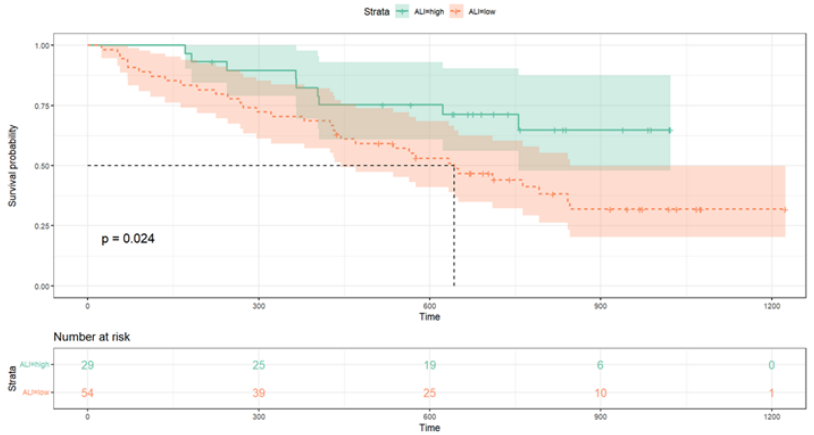

## ALI (auto) + TMTV



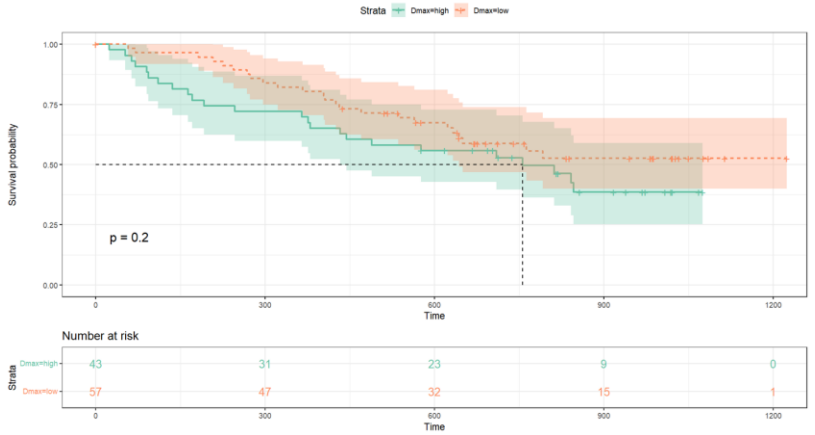

## ALI (auto) + Dmax



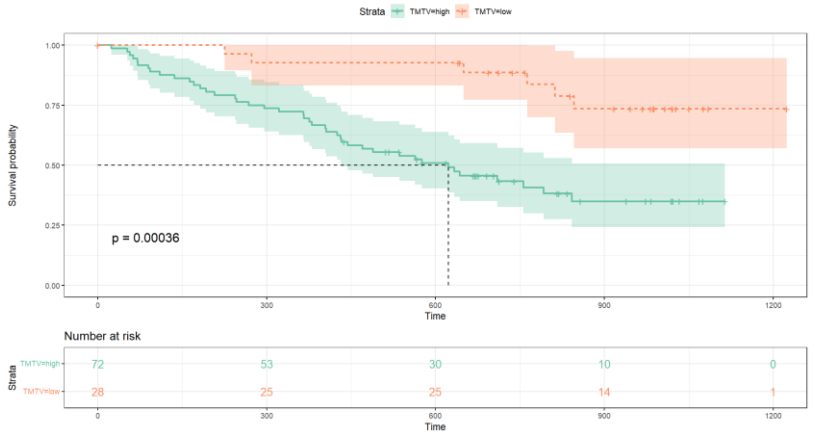

## ALI (auto)




## Dmax (auto)

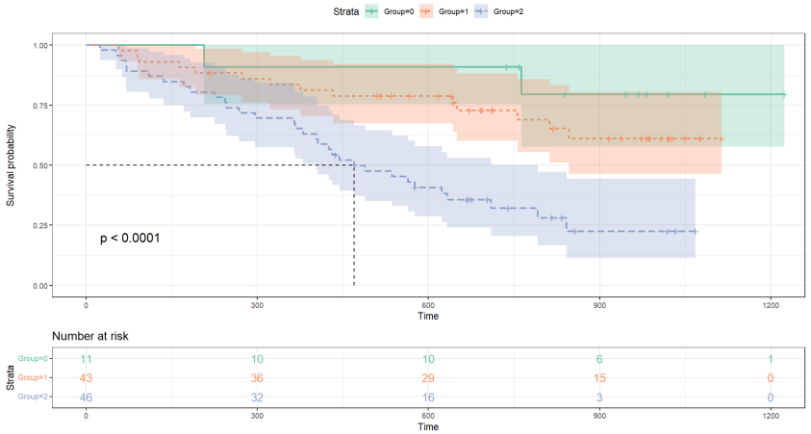



## TMTV (auto)

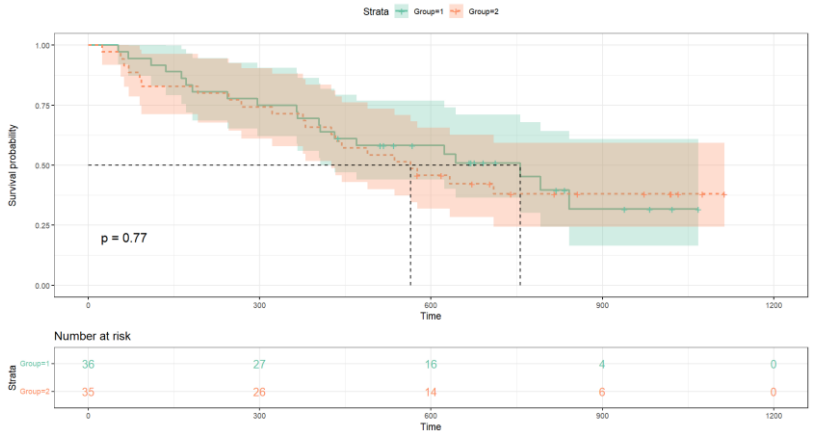


# Comparaisons des modèles: TIPIT

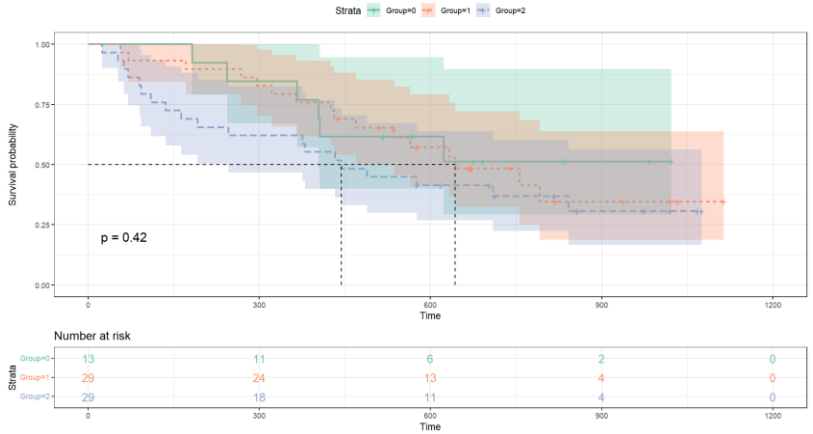
**TMTV + BMI + Age**




**ALI (auto) + TMTV**



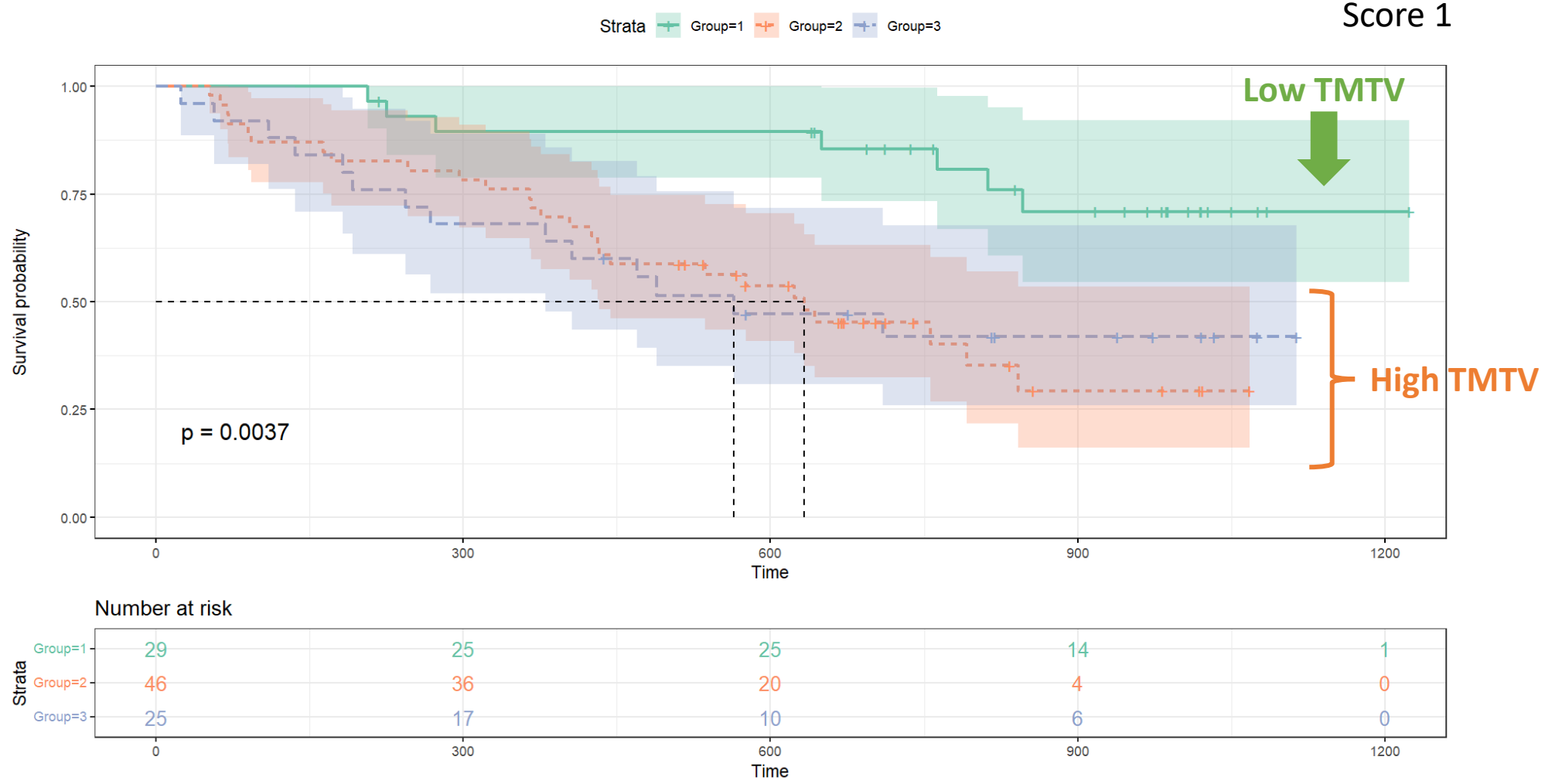

**ALI (auto) + Dmax**



# Comparaisons des modèles: TIPIT

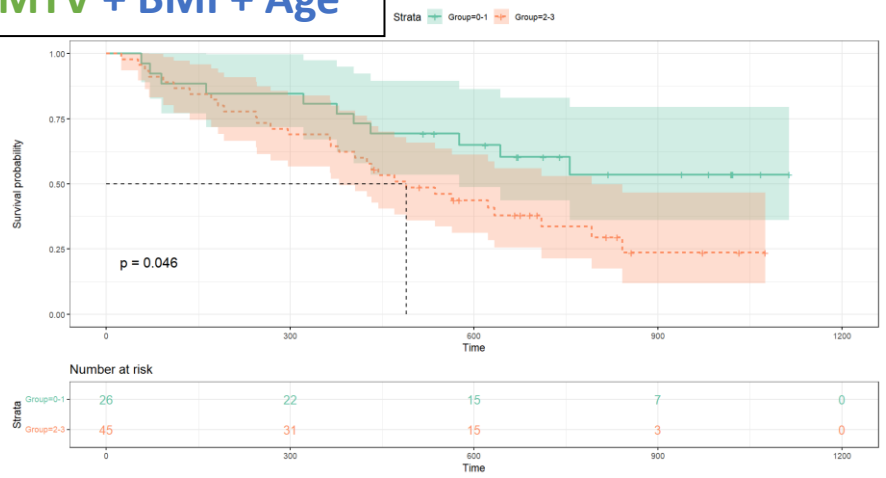
→ par clustering (modèle de régression par classes latentes, méthode STARS)

Score 1



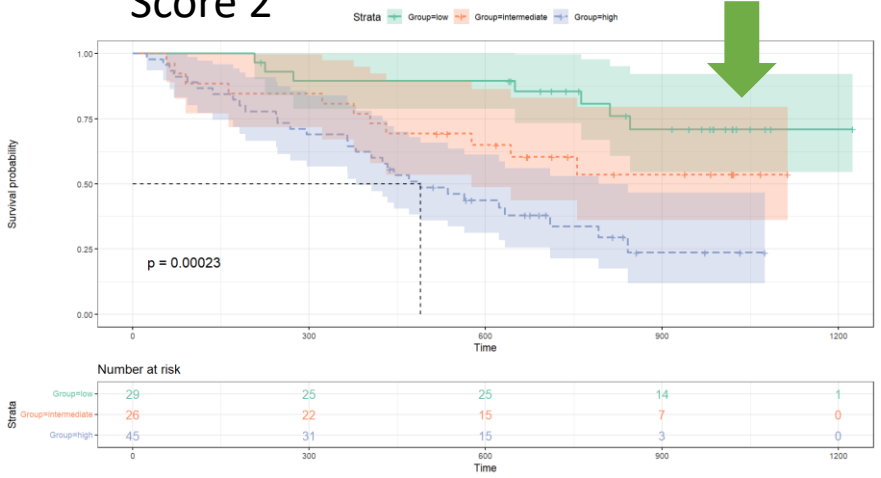
# Comparaisons des modèles: TIPIT

**TMTV + BMI + Age**

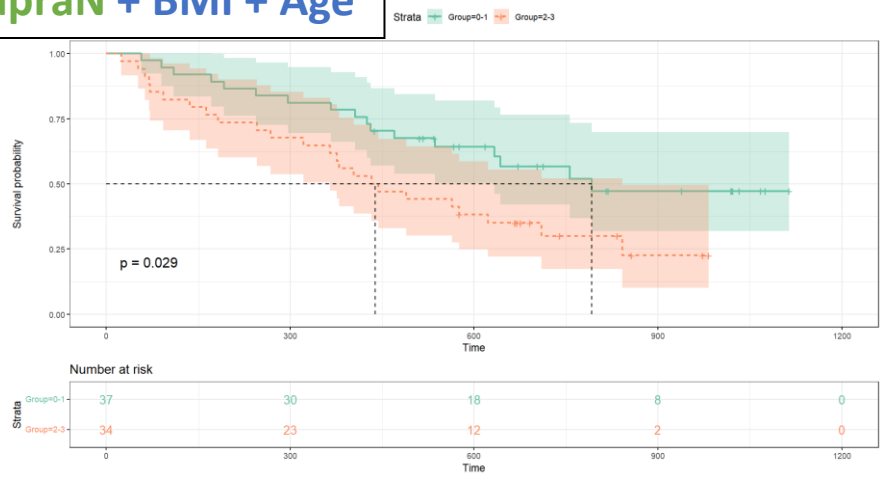



Score 2

Low TMTV

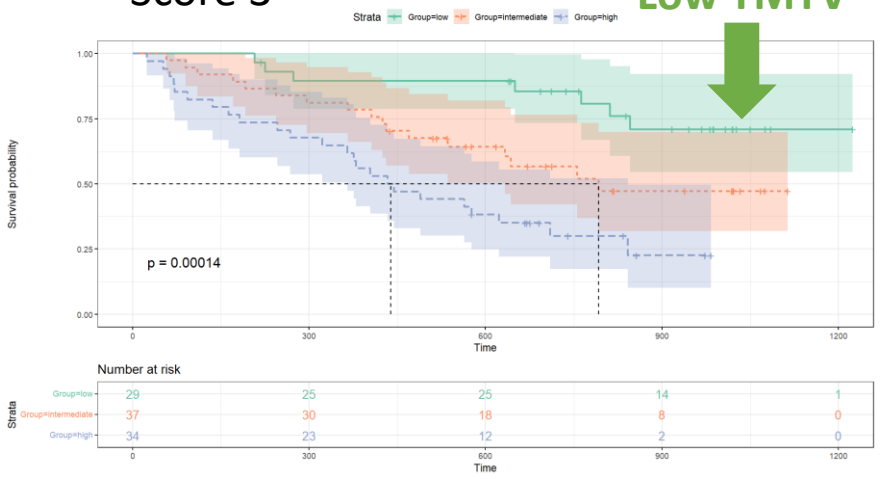



**SupraN + BMI + Age**



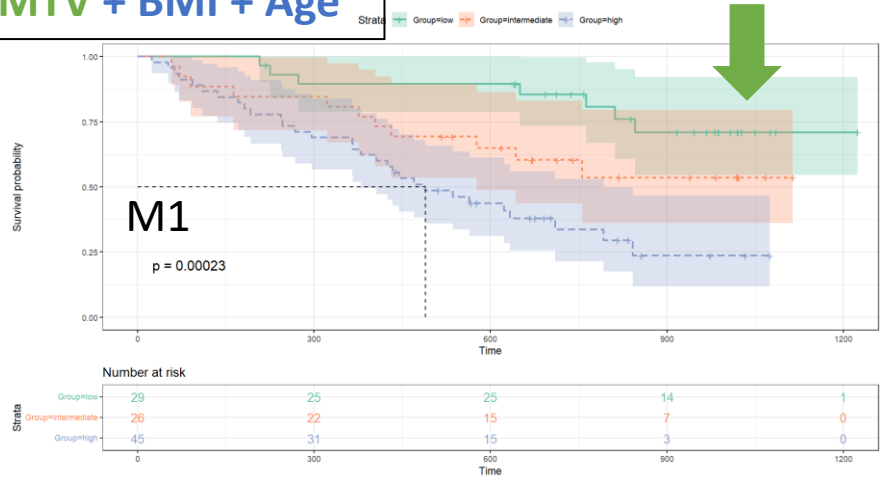

Score 3

Low TMTV

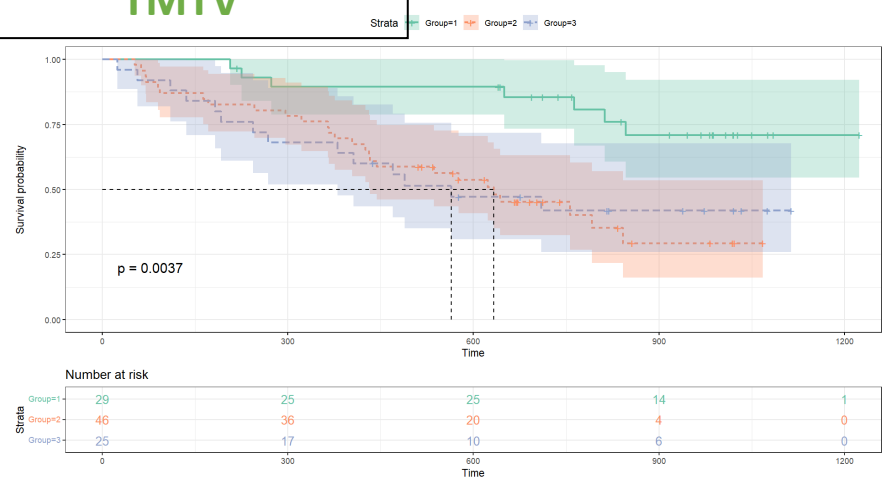


# Comparaisons des modèles: TIPIT

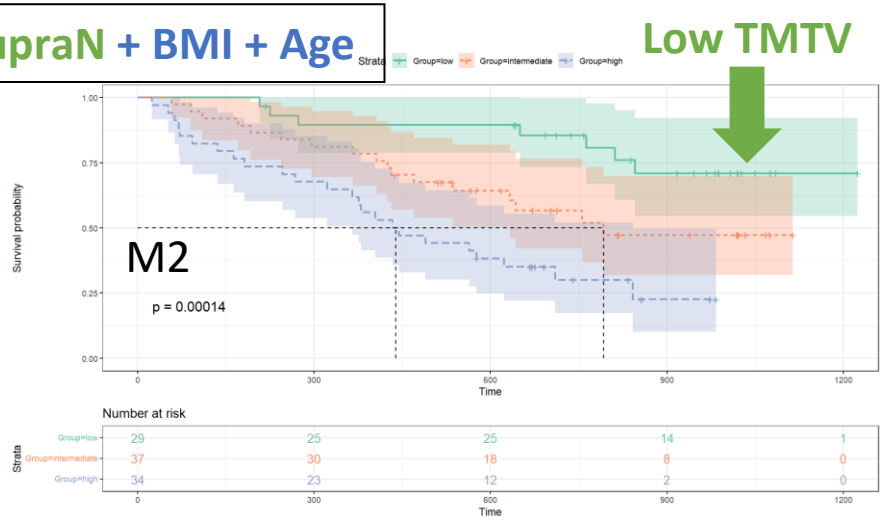
**TMTV + BMI + Low TMTV**




**TMTV**



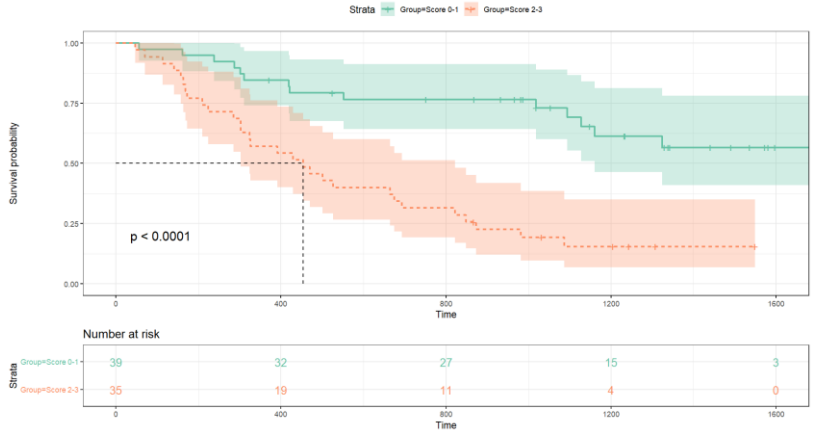

**SupraN + BMI + Low TMTV**



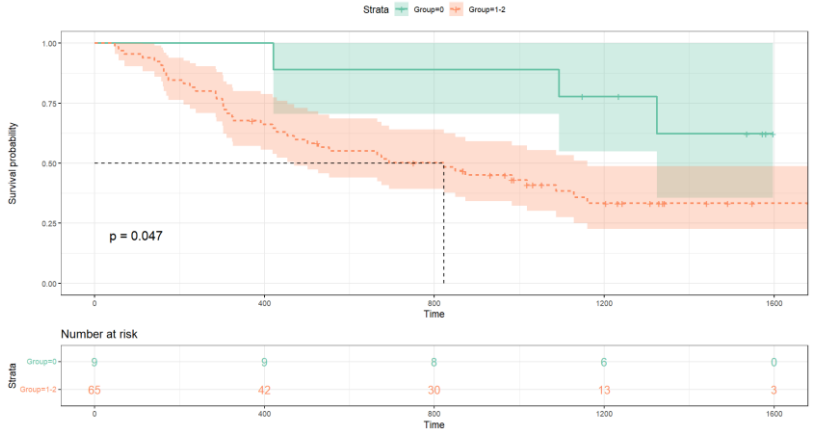

| Models | C-index | HR [CI] | p (Wald test) |
|---|---|---|---|
| TMTV | **0.627** | 1.668 [1.449 -2.422] | 7.11E-03 |
| M1 | 0.522 | 1.159 [0.828 – 1.623] | 3.89E-01 |
| M2 | 0.516 | 0.878 [0.602 – 1.28] | 5.00E-01 |

# Comparaisons des modèles: Capricorne

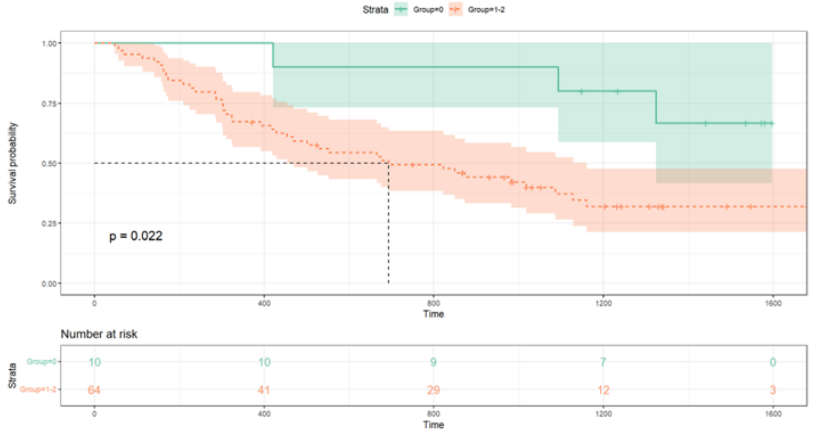
## TMTV + Dmax + Age




## ALI (auto) + Dmax

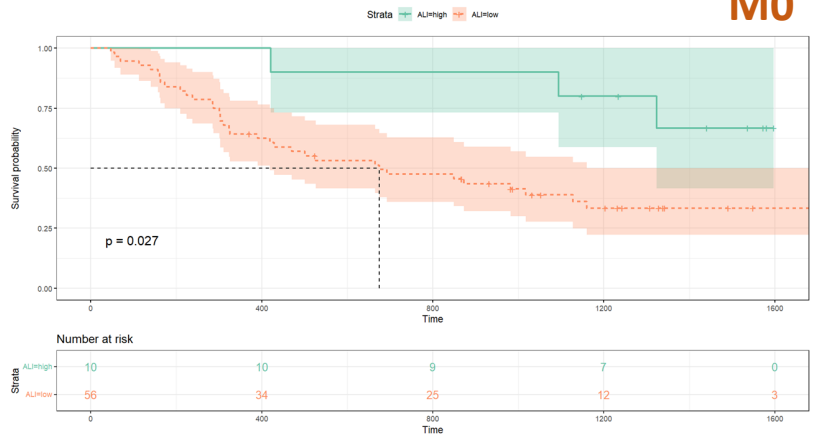



## ALI (auto) + TMTV

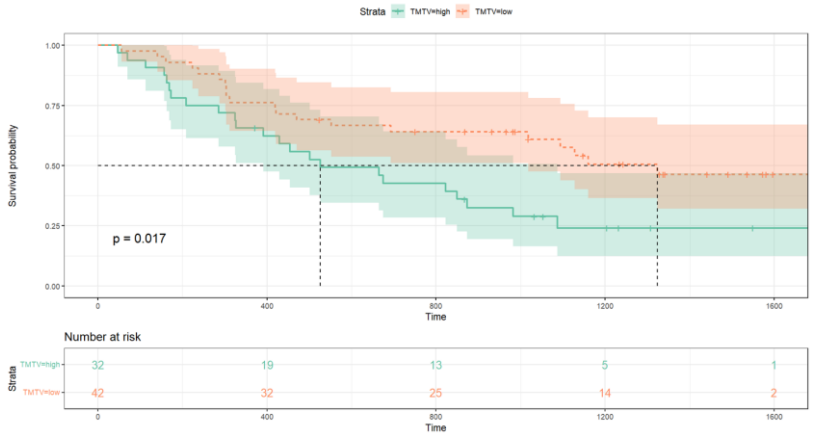



## ALI (auto)

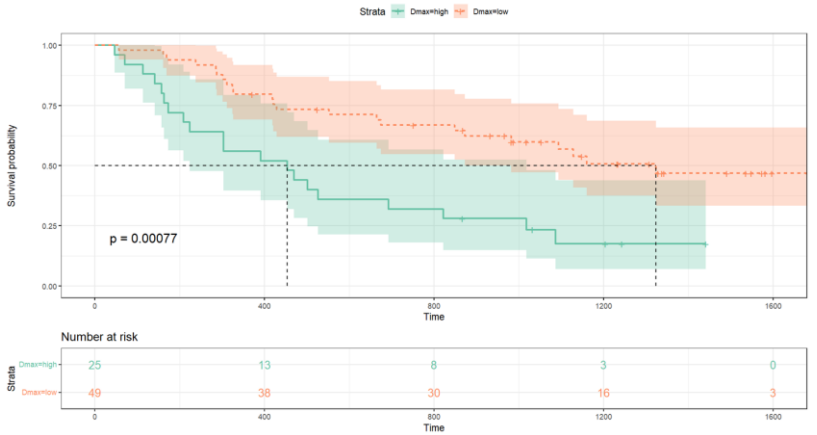
M0




## TMTV (auto)



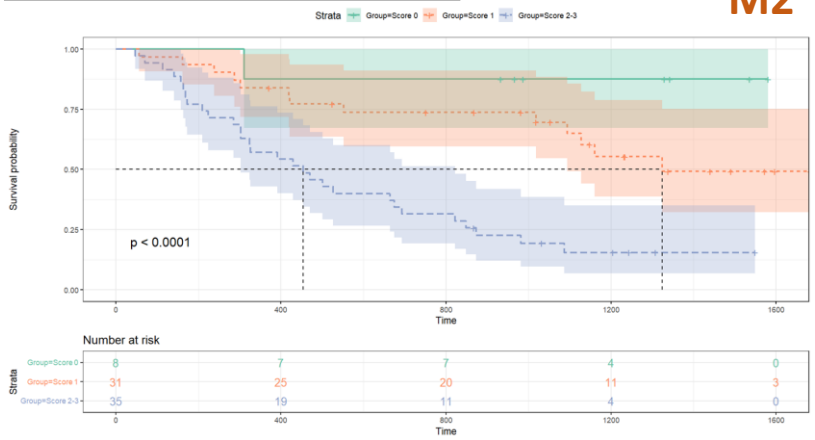

## Dmax (auto)



# Comparaisons des modèles: Capricorne

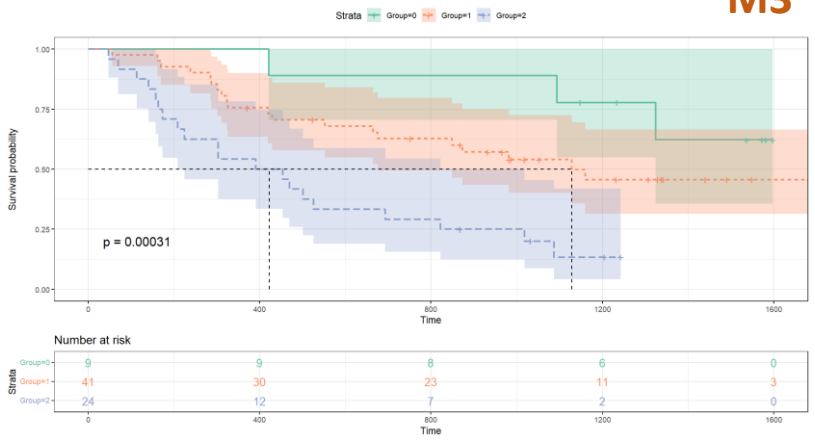
## TMTV + Dmax + Age

M2



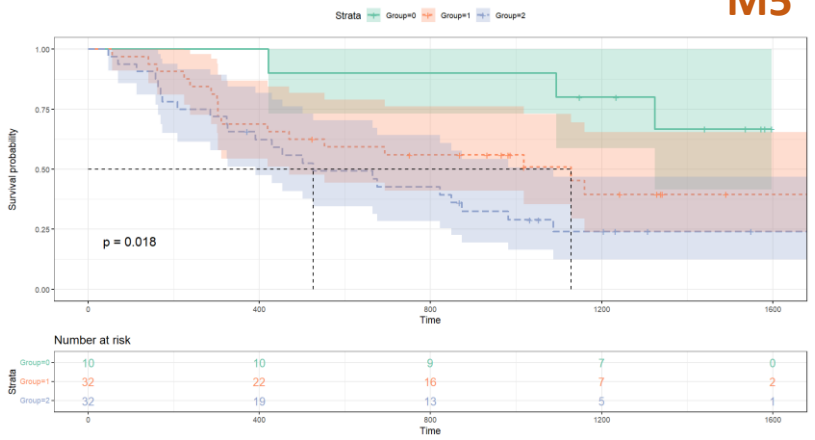

## ALI (auto) + Dmax

M3



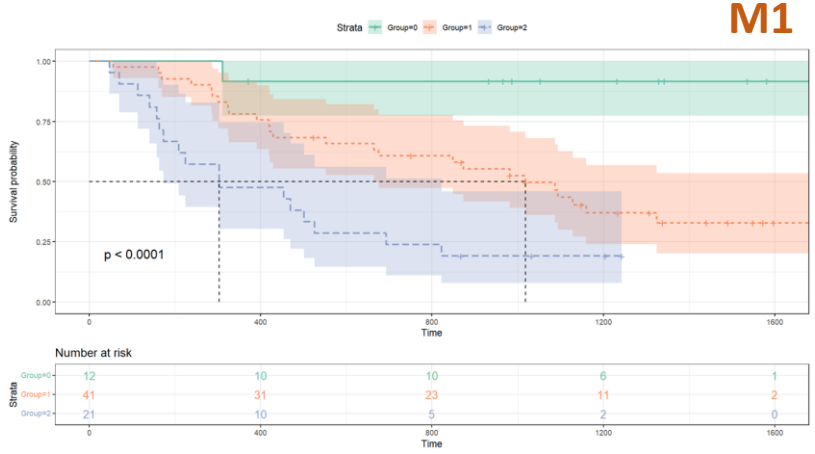

## ALI (auto) + TMTV

M5



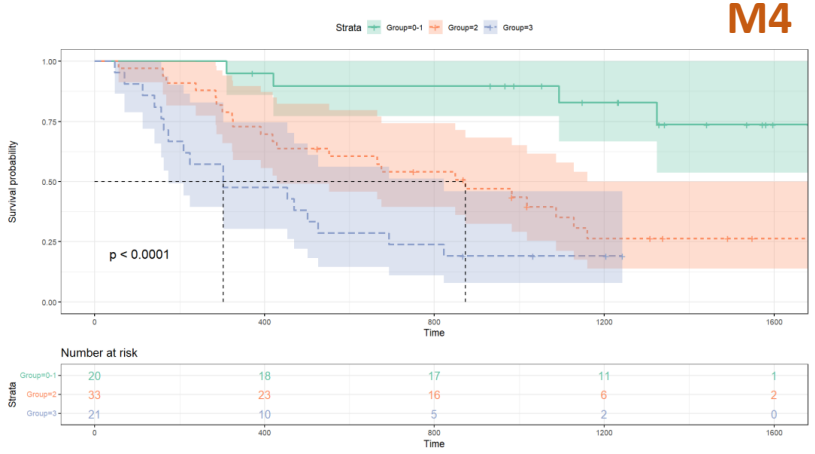

## Dmax + Age

M1



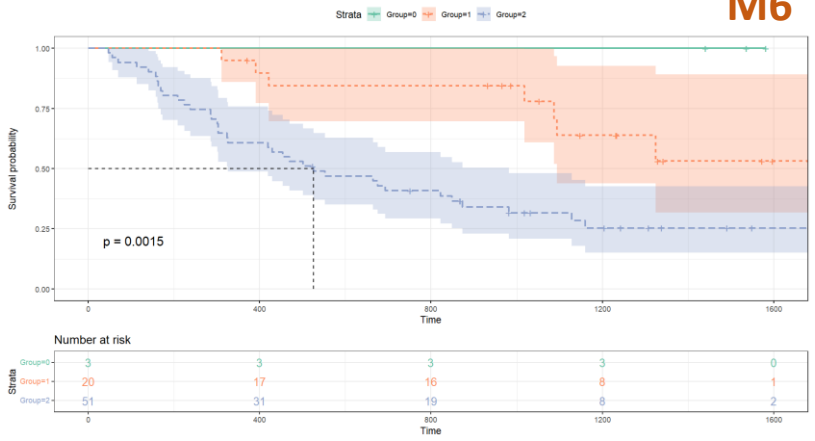

## ALI (auto) + Dmax + Age

M4




## ALI (auto) + Age

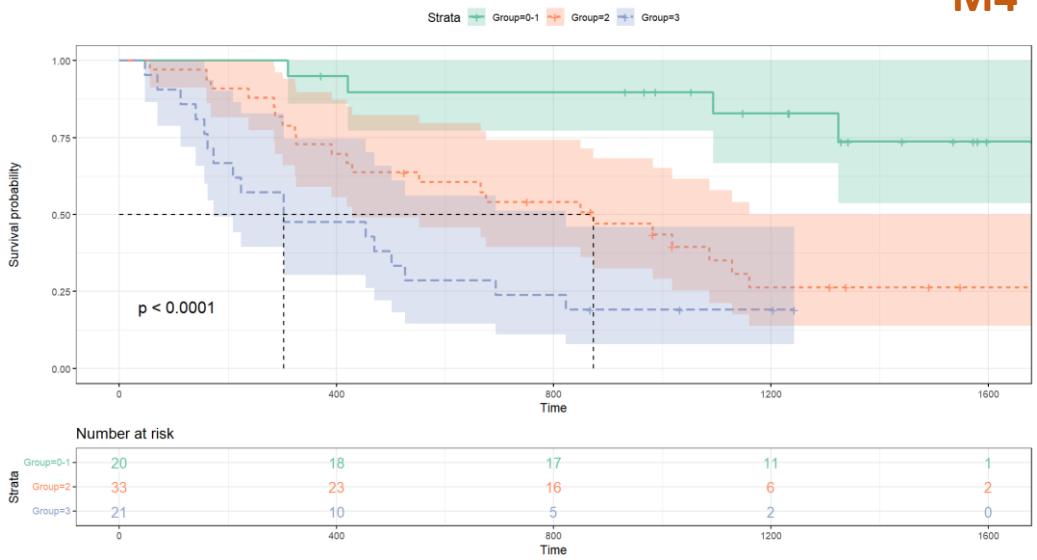
M6



# Comparaisons des modèles: Capricorne

**ALI (auto) + Dmax + Age**

**M4**




| Models | C-index | HR | p (Wald test) |
|---|---|---|---|
| ALI > 42.4 | **0.575** | 0.275 [0.084 - 0.896] | 3,22E-02 |
| Age < 60 | 0.6 | **0.256 [0.091 - 0.718]** | 9,58E-03 |
| TMTV < 90 | 0.589 | 0.484 [0.264 - 0.889] | 1,92E-02 |
| Dmax < 28.4 | 0.624 | 0.367 [0.290 - 0.673] | 1,21E-03 |
| M1 | 0.681 | 0.328 [0.196 - 0.549] | 2,18E-05 |
| M2 | 0.679 | 0.292 [0.163 - 0.522] | 3,32E-05 |
| M3 | 0.661 | 0.381 [0.229 - 0.637] | 2,25E-04 |
| M4 | **0.708** | 0.366 [0.235 - 0.568] | **7,64E-06** |
| M5 | 0.619 | **0.522 [0.329 - 0.828]** | 5,70E-03 |
| M6 | 0.65 | 0.273 [0.126 - 0.591] | 9,72E-04 |

→ Le modèle M4 est sigificativement différent de tous les autres modèles sauf M1 (Dmax + Age) et M2 (TMTV + Dmax + Age).

# Conclusions:

**TIPIT** : work in progress…

✓ Déterminer d'autres modèles basés sur le TMTV et autres paramètres radiomiques et/ou cliniques

**Capricorne** :

✓ Score ALI amélioré par la combinaison de paramètres radiomiques simples et de l'âge

✓ Work in pogress:

- Définir les autres modèles pouvant être générés à partir du Dmax, du TMTV et de l'âge
- Déterminer quel est le modèle prédictif de la survie globale
- Abstract