

Against toxicity prediction tools in current practice

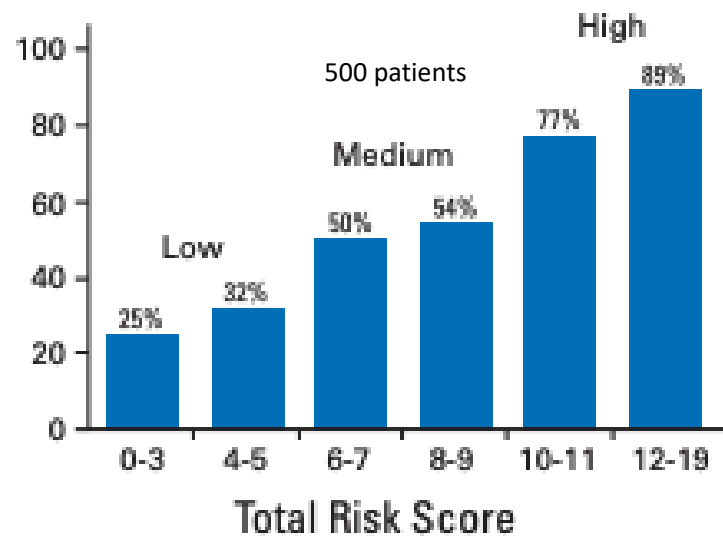
JOURNÉE SCIENTIFIQUE DIALOG DU 25 MAI 2023

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Predictivity of these
scores

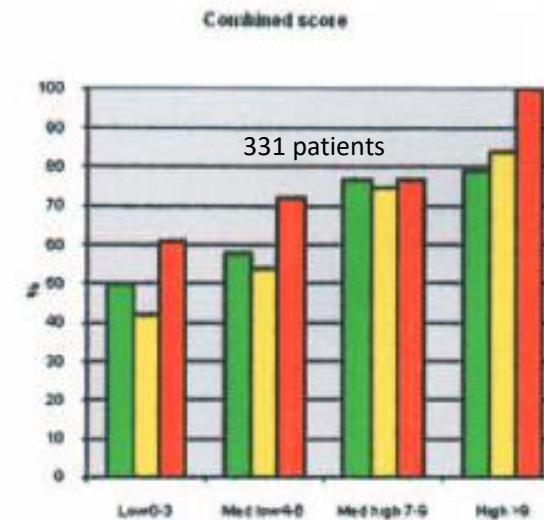
C-scores in development cohorts

CARG Score



C-Score=0,72

CRASH Score



C-Score=0,65

C-Scores in external cohorts

| | Nb of patients | C-Score for CARG | C-Score for CRASH |
|---|----------------|------------------|-------------------|
| Hurria et al. JCO 2016 | 250 | 0.65 | |
| Alibhai et al JGO 2017 | 46 | 0.64 | |
| Kotzerke et al. JGO 2019 | 104 | 0.78 | |
| Moth et al. JGO 2019 | 126 | 0.52 | |
| Zhang et al. Oncol Lett. 2019 | 106 | 0.77 | 0.76 |
| Feliu et al. Oncologist 2020 | 551 | 0.54 | |
| Ortland et al. JGO 2020 | 120 | 0.68 | 0.65 |
| Ostwal et al. BMJ Open 2021 | 270 | 0.63 | |
| Pang et al. JAMA Netw Open 2022 | 200 | 0.74 | |
| Boudou-Rouquette et al. Clin Nutr. 2022 | 179 | 0.57 | 0.51 |
| Frelaut et al. Oncologist 2023 | 248 | 0.55 | 0.52 |

Components of these
scores

Partial thresholds

| Risk Factor | Prevalence | | Grades 3 to 5 Toxicity | | OR | 95% CI | Score |
|---|------------|----|------------------------|----|------|--------------|-------|
| | No. | % | No. | % | | | |
| Age ≥ 72 years | 270 | 54 | 163 | 60 | 1.85 | 1.22 to 2.82 | 2 |
| Cancer type GI or GU | 185 | 37 | 120 | 65 | 2.13 | 1.39 to 3.24 | 2 |
| Chemotherapy dosing, standard dose | 380 | 76 | 204 | 54 | 2.13 | 1.29 to 3.52 | 2 |
| No. of chemotherapy drugs, polychemotherapy | 351 | 70 | 192 | 55 | 1.69 | 1.08 to 2.65 | 2 |
| Hemoglobin < 11 g/dL (male), < 10 g/dL (female) | 62 | 12 | 46 | 74 | 2.31 | 1.15 to 4.64 | 3 |
| Creatinine clearance (Jelliffe, ideal weight) < 34 mL/min | 44 | 9 | 34 | 77 | 2.46 | 1.11 to 5.44 | 3 |
| Hearing, fair or worse | 123 | 25 | 76 | 62 | 1.67 | 1.04 to 2.69 | 2 |
| No. of falls in last 6 months, 1 or more | 91 | 18 | 61 | 67 | 2.47 | 1.43 to 4.27 | 3 |
| IADL: Taking medications, with some help/unable | 39 | 8 | 28 | 72 | 1.50 | 0.66 to 3.38 | 1 |
| MOS: Walking 1 block, somewhat limited/limited a lot | 109 | 22 | 69 | 63 | 1.71 | 1.02 to 2.86 | 2 |
| MOS: Decreased social activity because of physical/emotional health, limited at least sometimes | 218 | 44 | 126 | 58 | 1.36 | 0.90 to 2.06 | 1 |

| Predictors | Points | | |
|--|--------|------------|-------|
| | 0 | 1 | 2 |
| Hematologic score^a | | | |
| Diastolic BP | ≤72 | >72 | |
| IADL | 26-29 | 10-25 | |
| LDH (if ULN 618 U/L; otherwise, 0.74 /L*ULN) | 0-459 | | >459 |
| Chemotox ^b | 0-0.44 | 0.45- 0.57 | >0.57 |
| Nonhematologic score^a | | | |
| ECOG PS | 0 | 1-2 | 3-4 |
| MMS | 30 | | <30 |
| MNA | 28-30 | | <28 |
| Chemotox ^b | 0-0.44 | 0.45-0.57 | >0.57 |

Variables including toxicity

| Risk Factor | Prevalence | | Grades 3 to 5 Toxicity | | OR | 95% CI | Score |
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Use in clinical practice

Only severe toxicities matter?

- Grade 3+ for CARG
- Grade 3+ non heme and Grade 4+ heme for CRASH
- Impact of non severe toxicities?
 - Fatigue, weight loss...
 - More specific: neuropathy and falls
 - Especially among older patients
- Every high grade toxicity is limiting?

| Event | Nivolumab plus Cabozantinib (N = 320) | | Sunitinib (N = 320) | |
|-----------|---------------------------------------|----------------|---------------------|----------------|
| | Any Grade | Grade ≥ 3 | Any Grade | Grade ≥ 3 |
| | <i>number of patients (percent)</i> | | | |
| Any event | 319 (99.7) | 241 (75.3) | 317 (99.1) | 226 (70.6) |

Cover every situation?

- 500/331 patients
- Vs. multiple treatment /oncologic features/ geriatric features combination
- Not consider specific risks (diabetes/osteoporosis and neuropathy)
- Developed only for chemotherapy
 - Targeted therapy?
 - Immunotherapy?
 - Combo?

| | | | |
|-------------------|--------------------|--------|-------------------------------|
| CTE 010 - ORL | DOCETAXEL | CHIP M | LV5FU2 PANITIMUMAB |
| CTE 031 - POU MON | DURVALUMAB | CISGEN | LV5FU2 AFLIBERCEPT |
| AMIVANTAMAB | DURVALUMAB C | DCF mc | LV5FU2 AVASTIN |
| ANCIENS PROTC | DURVALUMAB C | ELOXA | LV5FU2 CARBO |
| ATEZOLIZUMAB | EN COURS OSE | FLOT | LV5FU2 CDDP |
| AVASTIN | GEMCITABINE | FOLFIR | LV5FU2 (INFUSEUR) |
| CAP | GEMCITABINE BI | FOLFIR | LV5FU2 OXALI IAH |
| CAP CARBO | GEMOX | FOLFIR | LV5FU2 OXALI IAH + AVASTIN |
| CARBO ETOPOS | LURBINECTEDIN | FOLFIR | LV5FU2 OXALI IAH + CETUXIMAB |
| CARBO ETOPOS | NIVOLUMAB | FOLFIR | MITOMICYNE IAH |
| CARBO ETOPOS | NIVOLUMAB - IPI | FOLFIR | NIVOLUMAB OESOPHAGE/ESTOMA |
| CARBO GEMCIT | PACLITAXEL | FOLFIR | PACLITAXEL INTRA- PERITONEAL |
| CARBO GEMCIT | PACLITAXEL BEV | FOLFIR | PANITIMUMAB |
| CARBO PACLITA | PAVEP | FOLFIR | PEMBROLIZUMAB AAP OESOPHAGE |
| CARBO PACLITA | PEMBROLIZUMAB | FOLFIR | PEMETREXED INTRA PERITONEAL |
| CARBO PACLITA | PEMETREXED | FOLFIR | PIPAC |
| CARBO PACLITA | PEMETREXED B | FOLFIR | TFOX |
| CARBO PACLITA | PEMETREXED P | FOLFIR | TOMOX |
| CARBO PEMETR | PROTOCOLES D | FOLFIR | TOMUDEX |
| CARBO PEMETR | TOPOTECAN | FOLFIR | TRASTUZUMAB |
| CARBO PEMETR | VINORELBINE | FOLFOX | TRASTUZUMAB DERUXTECAN AAP |
| CARBO VINDRELE | VIP | FOLFOX | TRASTUZUMAB FOLFOX |
| CAV | CTE 041 - DIGESTIF | FOLFOX | XELIRI |
| CDDP ETOPOSIC | ATEZOLIZUMAB | FOLFOX | XELIRI AVASTIN |
| CDDP GEMCITAI | BEVACIZUMAB | FOLFOX | XELODA |
| CDDP GEMCITAI | CAMPTO | FOLFOX | XELODA AVASTIN |
| CDDP PEMETRE | CAMPTO CETUX | FOLFOX | XELODA CDDP HERCEPTINE |
| CDDP PEMETRE | CARBO PACLITA | GEMCI | XELODA MITOMYCINE CONCO RT |
| CDDP PEMETRE | CDDP 5FU | GEMCI | XELOX |
| CDDP VINDRELE | CETUXIMAB | GEMCI | XELOX AVASTIN |
| CDDP VINDRELE | CHIP | GEMOX | 5FU MITOMYCINE CONCOMITANT RT |
| CEMPIIMAB | CHIP DOXORUBI | IRINOT | CTE 050 - SEIN |
| DOCETAXEL | | LV5FU | ATEZOLIZUMAB PACLITAXEL |

Decision of treatment in (geriatric) oncology

- Depends on benefit/risk ratio
- Will we tolerate the same risk depending on the situation
 - Metastatic pancreas vs High grade Lymphoma?

