DIALOG
Gerico · Ucog

Against toxicity prediction tools in current practice

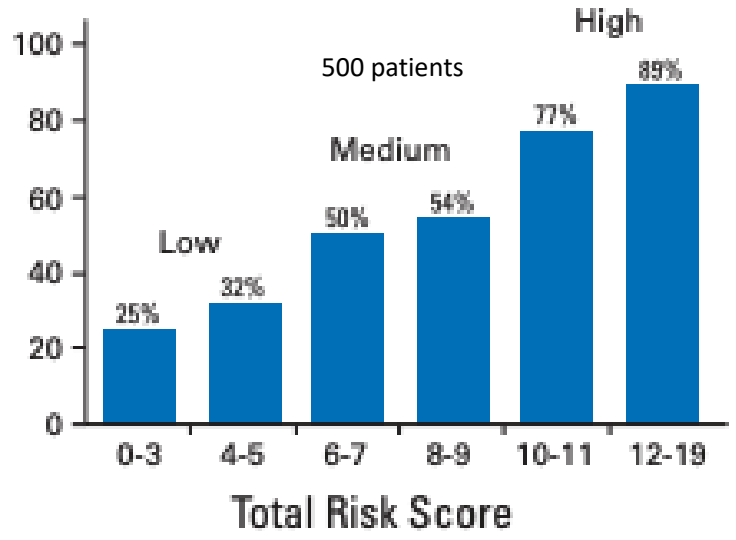
JOURNÉE SCIENTIFIQUE DIALOG DU 25 MAI 2023

PHILIPPE CAILLET & MAXIME FRÉLAUT

Predictivity of these scores

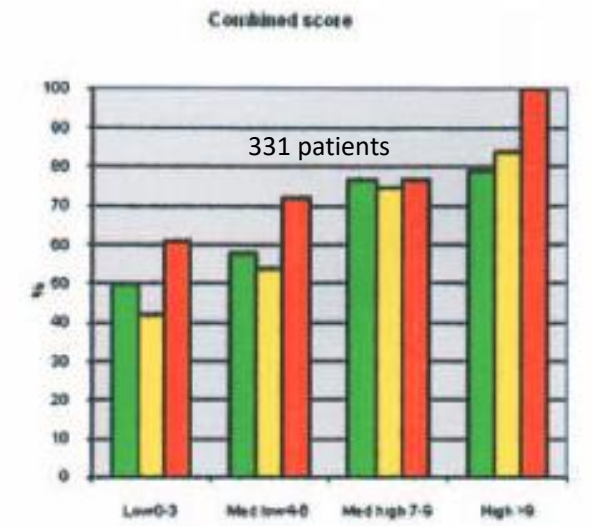
C-scores in development cohorts

CARG Score



C-Score=0,72

CRASH Score



C-Score=0,65

Hurria et al. JCO 2011
Extermann et al. Cancer 2012

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 No.	Prevalence %	Grades 3 to 5 Toxicity No.	Grades 3 to 5 Toxicity %	OR	95% CI	Score
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

Hurria et al. JCO 2011
Extermann et al. Cancer 2012

Variables including toxicity

Risk Factor	Prevalence No.	Prevalence %	Grades 3 to 5 Toxicity No.	Grades 3 to 5 Toxicity %	OR	95% CI	Score
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

Hurria et al. JCO 2011
Extermann et al. Cancer 2012

Use in clinical practice

Only severe toxicities matter?

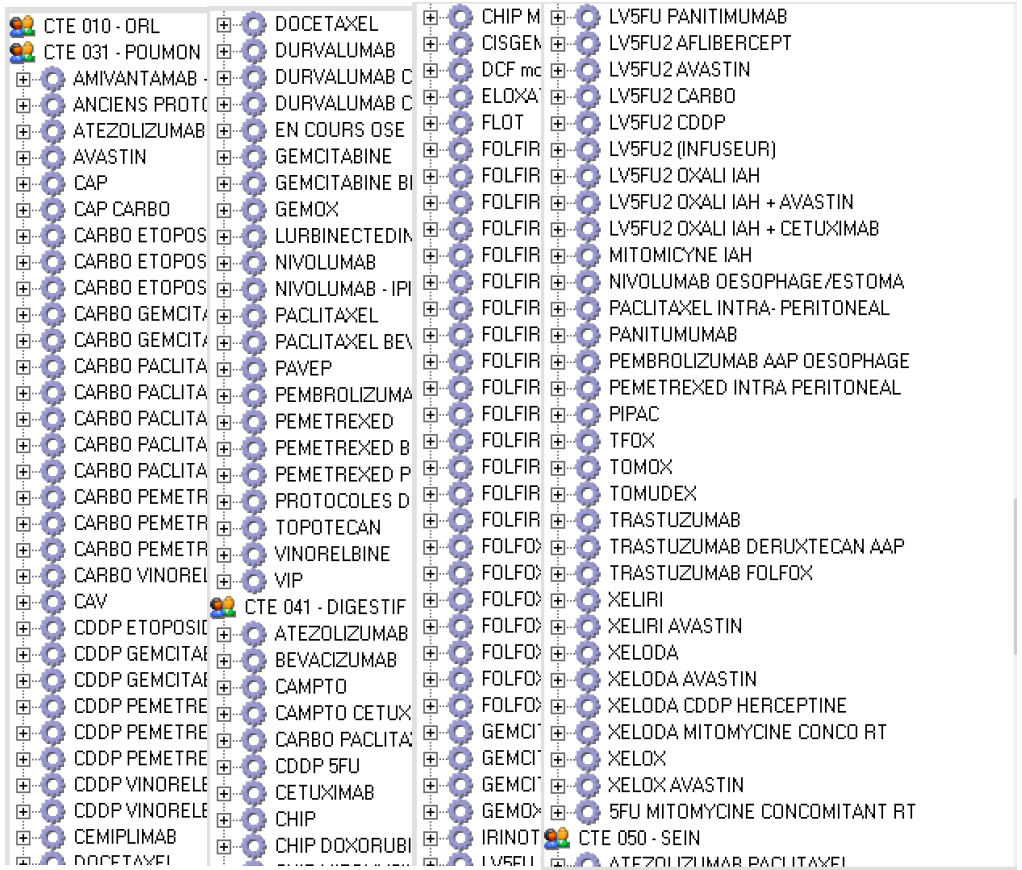
- Grade 3+ for CARG
- Grade 3+ non heme and Grade 4+ heme for CRASH
- Impact of non severe toxicities?
  - Fatigue, weight loss…
  - More specific: neuropathy and falls
  - Especially among older patients
- Every high grade toxicity is limiting?

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

Choueiri et al. NEJM 2021

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?



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?