

PRO toxicity prediction tools in current practice

Dr Rabia Boulahssass – geriatrician CHU Nice

Dr Camille Chakiba- medical oncologist- Institut Bergonié Bordeaux



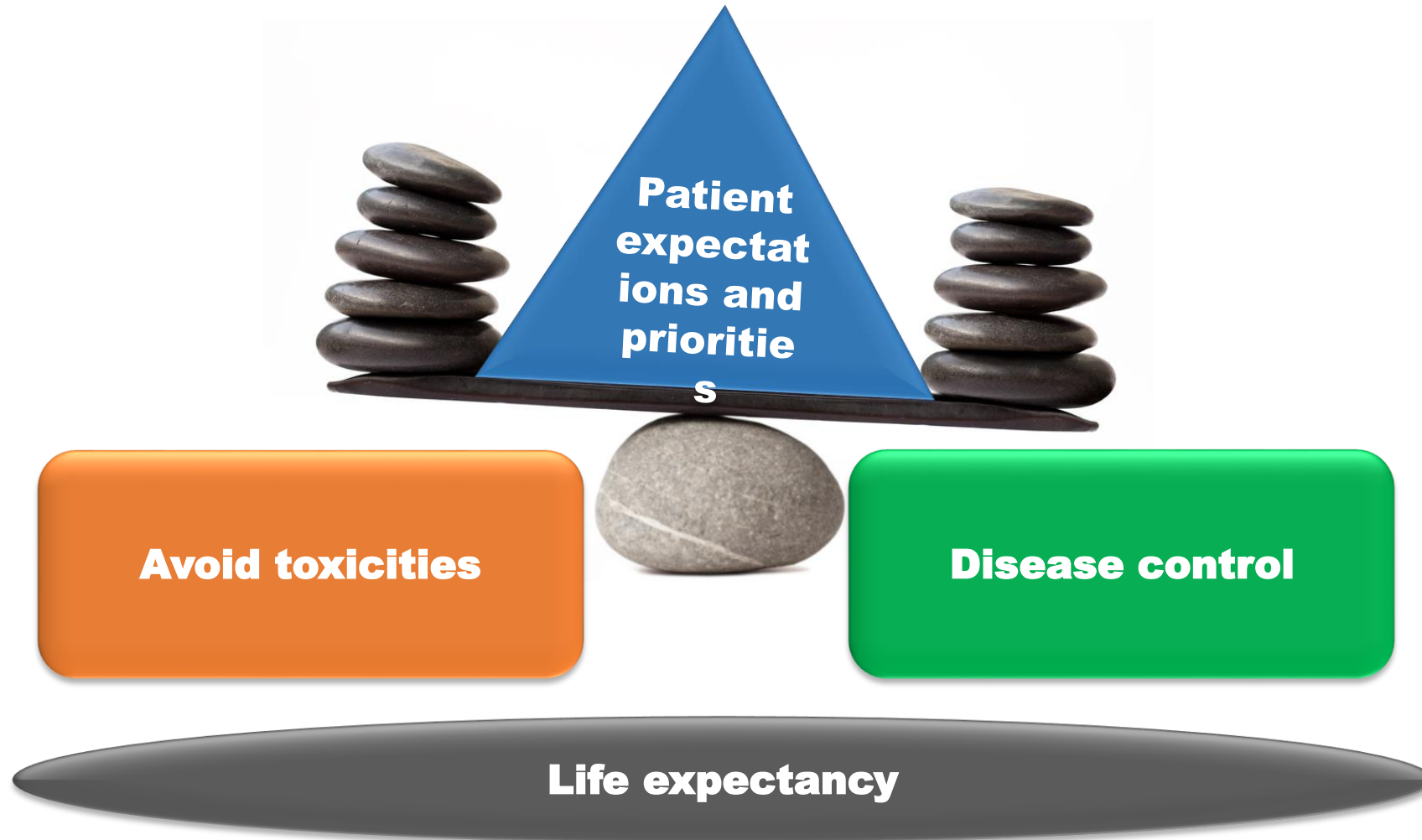
Clinical case number 1: 84 year old woman

- **31-03-20**: mastectomy- lymph nodes dissection:
CCI 30 mm, grade III, triple negative, Ki67 80%, 2/10N+. R0.
- Comorbidities: hypertension, atrial fibrillation, arthrosis, cataract
- 1m67, 67kg
- Treatments : FLECAINE, BISOPROLOL, XARELTO, MANIDIPINE,
ENLAPRIL + HYDROCHLOROTHIAZIDE, OMEPRAZOLE, BROMAZEPAM,
EDUCTYL, KLIPAL CODEINE
- G8 13.5/17
- lives alone at home, independent

Clinical case number 2: 70 year old woman

- December 2022 : lumpectomy – SN: CCI 36 mm, grade III, luminal B, Her2 negative. 1/3 N+. R0.
- Comorbidities :
 - Mitral and aortic heart valve replacement.
 - Tricuspid valve replacement planned
 - Moderate heart failure (LVEF november 2022: 44%.)
 - Hypertension
 - Atrial fibrillation
- Treatments : BISOPROLOL, COUMADINE, FUROSEMIDE, RAMIPRIL
- G8: 14/17
- Lives with her husband, independent

What do we want for these patients ?





Scores , Scales are central to our geriatric activity

CORNELL,GDS15,GDS30,HAMILTON

ZARIT

TMTA,TMTB, Grober et Buchske , DMS 48, EMPAN,
ADAScog,BREF,WAIS

Tinetti ,Walking and Talking test...

GERONTE,AGGIR,IOWA

EVA, DOLOPLUS,ECPA



CARG

1.4 min

CRASH

3 min

A black and white photograph of a person in a dark suit, white shirt, and striped tie. Instead of a head, there is a large, round, black clock face. The clock shows the time as approximately 12:25. The background is a light-colored, textured wall.

Not so long for a trained healthcare professional !
....After a CGA

Predicting Chemotherapy Toxicity in Older Adults With Cancer: A Prospective Multicenter Study

Arti Hurria, Kayo Togawa, Supriya G. Mohile, Cynthia Owusu, Heidi D. Klepin, Cary P. Gross, Stuart M. Lichtman, Ajeet Gajra, Smita Bhatia, Vani Katheria, Shira Klapper, Kurt Hansen, Rupal Ramani, Mark Lachs, F. Lennie Wong, and William P. Tew

A B S T R A C T

Original Article

Predicting the Risk of Chemotherapy Toxicity in Older Patients: The Chemotherapy Risk Assessment Scale for High-Age Patients (CRASH) Score

Martine Extermann, MD¹; Ivette Boler, ARNP¹; Richard R. Reich, PhD^{1,2}; Gary H. Lyman, MD³; Richard H. Brown, MD⁴; Joseph DeFelice, MD^{5†}; Richard M. Levine, MD⁶; Eric T. Lubiner, MD⁷; Pablo Reyes, MD⁸; Frederic J. Schreiber III, MD⁹; and Lodovico Balducci, MD¹

500 pts

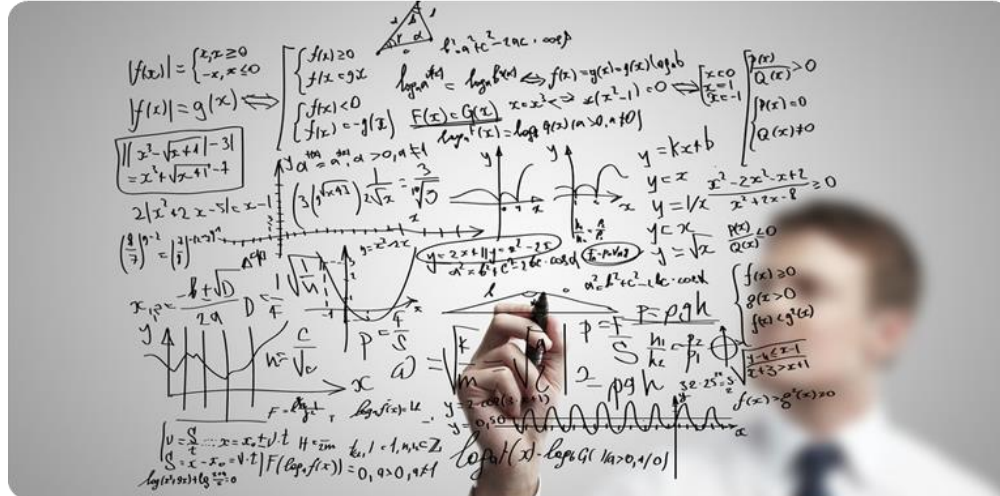
562 pts accrued

518 pts were split randomly into a derivation cohort and a validation

METHODOLOGY

STEP 1: Select the risk factors

Multivariate logistic regression



STEP 3: **Score points** were assigned to each risk factors by using the β **coefficient**

STEP 4: **The Discrimination**
The **accuracy** was assessed with the **mean c-Statistic**

STEP 2: The **Internal Validation**: 10-fold cross-validation process (**CARG**)
And **Bootstrapp** (**CRASH**)

STEP 5: **The Calibration**:
The Hosmer-Lemeshow **goodness of fit test**

STEP 5: External Validation

VOLUME 34 · NUMBER 20 · JULY 10, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

CRASH : external validation cohort n=187

Validation of a Prediction Tool for Chemotherapy Toxicity in Older Adults With Cancer

Arti Hurria, Supriya Mohile, Ajeet Gajra, Heidi Klepin, Hyman Muss, Andrew Chapman, Tao Feng, David Smith, Can-Lan Sun, Nienke De Glas, Harvey Jay Cohen, Vani Katheria, Caroline Doan, Laura Zavala, Abrahm Levi, Chie Akiba, and William P. Tew

Arti Hurria, Tao Feng, David Smith,
Can-Lan Sun, Vani Katheria, Caroline Doan,
Laura Zavala, Abrahm Levi, and Chie Akiba

A B S T R A C T

But also by other authors in different populations and countries..... CARG ++++

Hirota et al cancers 2022 Japan n= 76 pts solid tumors , 56% > 70yo

Cavdar et al JGO Turkey n=208 med age: 70yo

Kotzertke et al Germany n=104 median age: 72yo

Mariano et al Canada n=199 <70yo, impact on the supportive care plan 38%

Pang et al Asian population n=200 med age : 74yo

Ostal et al India n=270 mean age 69 ans.

Used in different localizations...

Alibhai ASCO 2019, cancer 2021

Metastatic castration resistant prostate cancer
CARG
71 pts

Nishijima et al , cancer 2022

Advanced noncolorectal GI cancers
Risk adapted CT based on the CARG score improved outcomes
50 pts

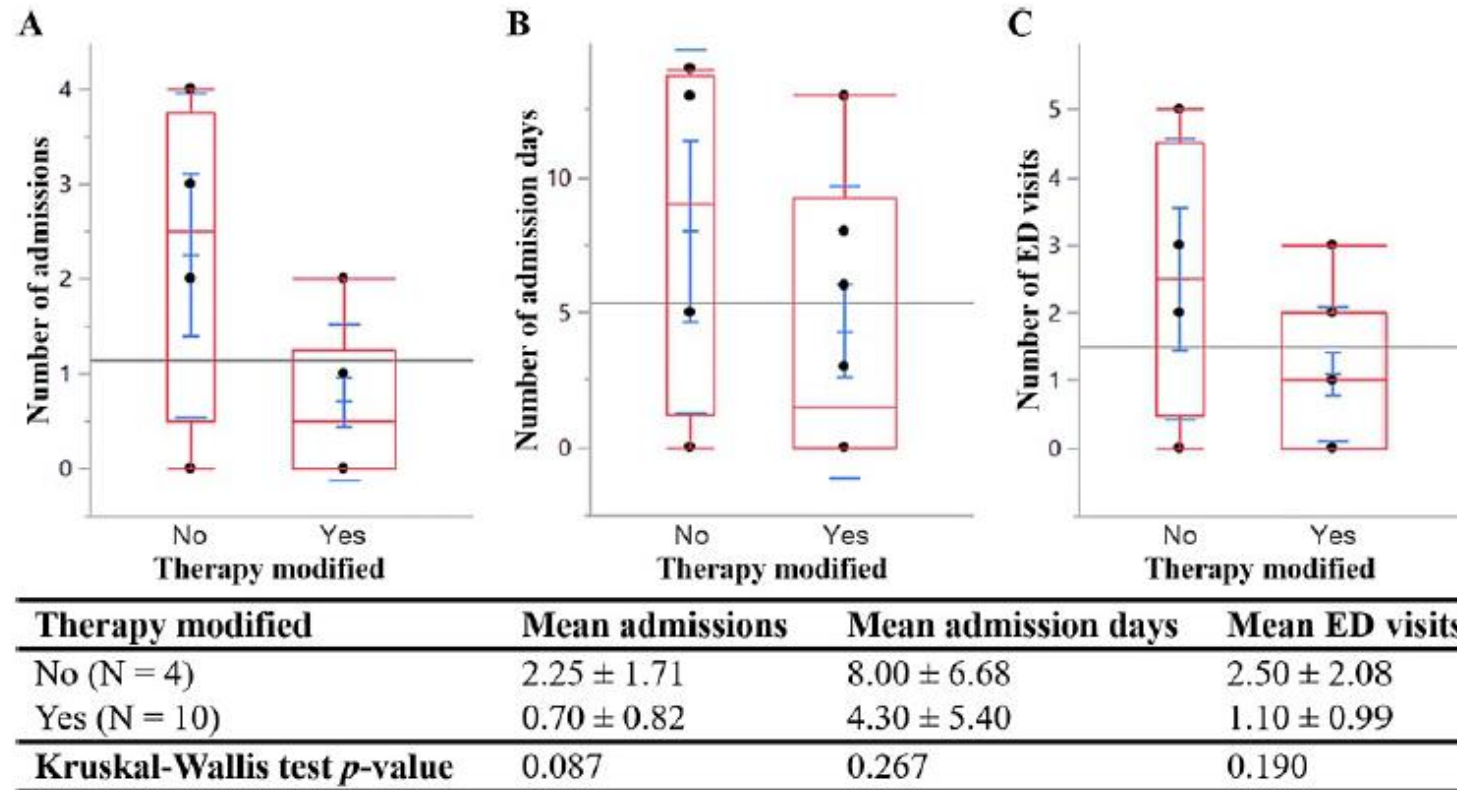
original reports **Development and Validation of a Risk Tool for Predicting Severe Toxicity in Older Adults Receiving Chemotherapy for Early-Stage Breast Cancer**

Allison Magnuson, DO¹; Mina S. Sedrak, MD²; Cary P. Gross, MD³; William P. Tew, MD⁴; Heidi D. Klepin, MD⁵; Tanya M. Wildes, MD⁶; Hyman B. Muss, MD⁷; Efrat Dotan, MD⁸; Rachel A. Freedman, MD⁹; Tracey O'Connor, MD¹⁰; William Dale, MD²; Harvey J. Cohen, MD¹¹; Vani Katheria, MS²; Anait Arsenyan, MS²; Abrahm Levi, BS²; Heeyoung Kim, MPH²; Supriya Mohile, MD¹; Arti Hurria, MD^{2,1}; and Can-Lan Sun, PhD²

TABLE 4. Cancer and Aging Research Group-Breast Cancer (CARG-BC) score calculator

Risk Predictor	Response	Score
Breast cancer stage	II or III	3
	I	0
Planned use of anthracyclines	Yes	1
	No	0
Planned treatment duration	> 3 months (12 weeks)	4
	≤ 3 months (12 weeks)	0
Hemoglobin	≤ 12 g/dL (female)	3
	≤ 13 g/dL (male)	
	> 12 g/dL (female)	0
	> 13 g/dL (male)	
Liver function	Abnormal LFTs, outside reference range	3
	Normal LFTs, within reference range	0
How many times have you fallen in the last 6 months?	≥ 1	4
	0	0
Does your health limit you in walking more than 1 mile?	Somewhat or very limited	3
	Not limited at all	0
How often is someone available to give you good advice about a crisis?	None, little, or some of the time	3
	Most or all of the time	0
	Total score:	

Using a chemotherapy Toxicity tool to decrease risks for hospitalization in older patients



For un busy oncologist ... CARG or CRASH? Index4 Tool ?

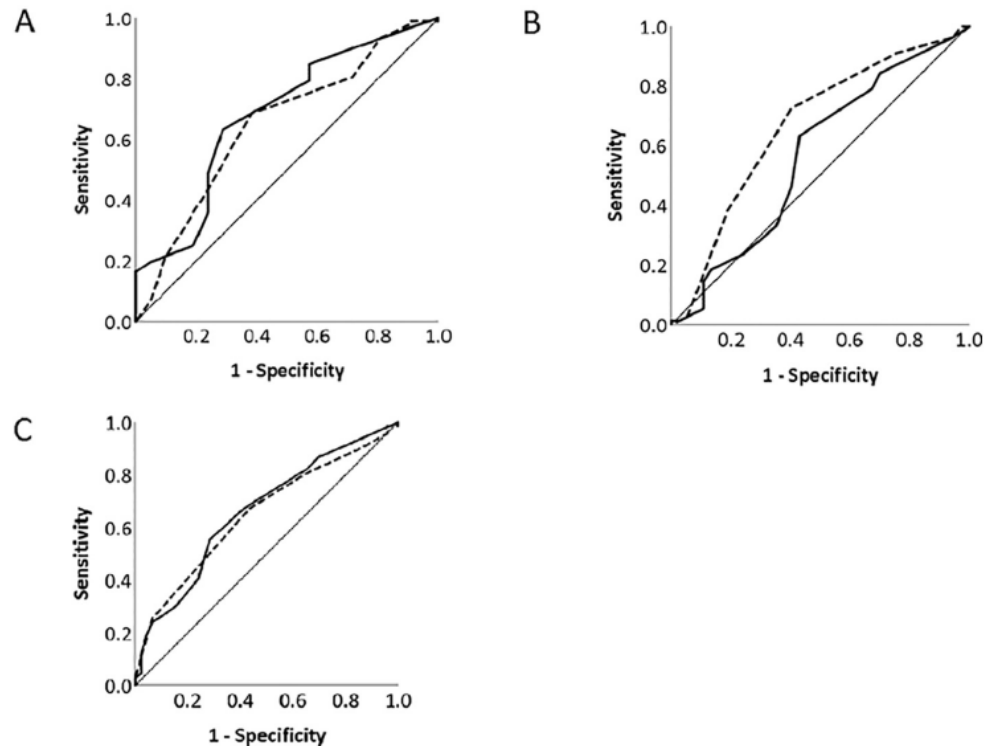


Fig. 3. ROC curves of the CARG and CRASH score for overall (A), hematologic (B) and nonhematologic (C) toxicity predictions. Solid line: CARG score, Dashed line: combined (A), hematologic (B) or nonhematologic (C) CRASH score.

Check for updates

OPEN



An evaluation of the Index4 tool for chemotherapy toxicity prediction in cancer patients older than 70 years old

Alexis Lewis¹, Melissa Reed¹, Natalie Walde¹ & Ioannis A. Voutsadakis^{2,3}✉

PS >1
Creatinine clearance
Albumin
Stage of cancer

Lewis scientific reports 2023

External Validity of Two Scores for Predicting the Risk of Chemotherapy Toxicity Among Older Patients With Solid Tumors: Results From the ELCAPA Prospective Cohort

Maxime Frelaut¹, , Elena Paillaud^{2,3}, Guillaume Beinse^{4,5}, Anne-Laure Scain⁶, Stéphane Culine^{7,8},
Christophe Tournigand⁹, Johanne Poisson^{3,10}, Sylvie Bastuji-Garin^{2,11},
Florence Canoui-Poitrine^{*,2,11,‡}, , Philippe Caillet^{‡,2,3,‡}

Limitations

- Adverse events were recorded retrospectively, (classification bias?).
- Proportion of missing data (especially for the CRASH score) → underestimate of the scores' predictive value through a lack of statistical power.
- Use of substitutive variables for 2 components of CARG score.
- Single-center mode of recruitment means that the predictive model lacks external validity.

Score de risque total du patient 6

Risque de toxicité pour le patient 44%

En utilisant le modèle prédictif de la toxicité liée au traitement chez les personnes âgées (Hurria et al, Journal of Clinical Oncology, 2011 ¹), ce patient a un risque 44% de toxicité de grade 3-5 ².

Facteur de toxicité / question	Valeur / Réponse	But
Âge du patient	Âge \geq 72	2
Type de cancer	Autre	0
Dosage	Dose réduite	0
Nombre d'agents de chimiothérapie	Dose standard	2
Hémoglobine	\geq 10 g/dL	0
Comment est votre ouïe (avec un appareil auditif, si nécessaire)?	Excellente	0
Combien de fois êtes-vous tombé(e) au cours des 6 derniers mois?	Aucun	0
Êtes-vous capable de prendre vous-même vos médicaments?	Sans aide (à la bonne dose et au bon moment)	0
Votre santé vous limite-t-elle à marcher un pâté de maisons (environ 100 mètres ou 300 pieds)?	Légèrement limité(e)	2
Au cours des 4 dernières semaines, combien de temps votre santé physique ou vos problèmes émotionnels ont-ils interféré avec vos activités sociales (comme rendre visite à des amis, des parents, etc.)?	Jamais	0
Clairance de la créatinine	58	0

Lactate dehydrogenase, U/L

0-459 U/L

0

>459 U/L

+2

Nonhematologic Score

Eastern Cooperative Oncology Group (ECOG) Performance Status

0 0

1-2 +1

3-4 +2

Mini Mental Health Status

30 0

<30 +2

Mini Nutritional Assessment

28-30 0

<28 +2

6 points

Combined score


Hematologic score: 3 points

Nonhematologic score: 5 points

Low-intermediate

Risk of severe toxicity

Copy Results 

Next Steps 

Chemotherapy risk
See chemotox table in [Evidence](#) for examples.

0 0	1 +1	2 +2
-----	------	------

Hematologic Score

Diastolic blood pressure, mmHg

≤72 mmHg	0
>72 mmHg	+1

Instrumental Activities of Daily Living score (IADL)

26-29 0	10-25 +1
---------	----------

Lactate dehydrogenase, U/L

0-459 U/L	0
>459 U/L	+2

Nonhematologic Score

Eastern Cooperative Oncology Group (ECOG)

6 points

Combined score
Hematologic score: 3 points
Nonhematologic score: 5 points

Low-intermediate

Risk of severe toxicity

Copy Results 📄

Next Steps >>>

Reset

Predict is not designed to be used in all cases. [Click here for more details.](#)

If you are unsure of any inputs or outputs, click on the **i** buttons for more information.

DCIS or LCIS only?



Yes No

Age at diagnosis



- 84 +

Age must be between 25 and 85

Post Menopausal?



Yes No Unknown

ER status



Positive Negative

HER2/ERRB2 status



Positive Negative Unknown

Ki-67 status



Positive Negative Unknown

Positive means more than 10%

Invasive tumour size (mm)



- 30 +

If there was more than one tumour, enter the size of the neo-adjuvant therapy was undertaken, enter the size of therapy.

Tumour grade



1 2 3

Detected by



Screening Symptoms Unknown

Positive nodes



- 2 +

Micrometastases only



Yes No Unknown

Enabled when positive nodes is 1.

Ki-67 status



Positive Negative Unknown

Positive means more than 10%

Micrometastases only



Yes No Unknown

Enabled when positive nodes is 1.

Treatment Options

Hormone Therapy



No **5 Years** 10 Years

Hormone (endocrine) therapy
Available when ER-status is positive

Chemotherapy



None 2nd gen **3rd gen**

Trastuzumab



No **Yes**

Available when HER2/ERRB2 status is positive

Bisphosphonates



No **Yes**

Available for post-menopausal women

Results

⚠ These results may be less accurate for women aged 70 and over

Table Curves Chart Texts **Icons**

Select number of years since surgery you wish to consider:

5 **10** 15

This display shows the number of women who survive at least 10 years after surgery.



- 63 deaths due to other causes
- 13 deaths related to breast cancer
- 2 extra survivors due to bisphosphonates
- 6 extra survivors due to chemotherapy
- 16 survivors with surgery alone

Patient number 1, 84 year old woman

- Adjuvant chemotherapy: 3EC75 with GCSF- 9 taxol + radiotherapy
- Good hematologic tolerance (but loss of 10 kg)
- Quick recovery from treatments but..
- 3 months after chemotherapy: fall at home, right hip fracture operated with prothesis
- Very good recovery
- 3 years after cancer diagnosis « lives normally » and cured from breast cancer (?)



Score de risque total du patient 4

Risque de toxicité pour le patient 30%

En utilisant le modèle prédictif de la toxicité liée au traitement chez les personnes âgées (Hurria et al, Journal of Clinical Oncology, 2011 ¹), ce patient a un risque 30% de toxicité de grade 3-5 ².

Facteur de toxicité / question	Valeur / Réponse	But
Âge du patient	Âge < 72	0
Type de cancer	Autre	0
Dosage	Dose réduite	0
Nombre d'agents de chimiothérapie	Dose standard	2
Hémoglobine	≥10 g/dL	0
Comment est votre ouïe (avec un appareil auditif, si nécessaire)?	Excellente	0
Combien de fois êtes-vous tombé(e) au cours des 6 derniers mois?	Aucun	0
Êtes-vous capable de prendre vous-même vos médicaments?	Sans aide (à la bonne dose et au bon moment)	0
Votre santé vous limite-t-elle à marcher un pâté de maisons (environ 100 mètres ou 300 pieds)?	Légèrement limité(e)	2
Au cours des 4 dernières semaines, combien de temps votre santé physique ou vos problèmes émotionnels ont-ils interféré avec vos activités sociales (comme rendre visite à des amis, des parents, etc.)?	Jamais	0
Clairance de la créatinine	68	0

Lactate dehydrogenase, U/L

0-459 U/L

0

>459 U/L

+2

Nonhematologic Score

Eastern Cooperative Oncology Group (ECOG) Performance Status

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1-2 +1

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6 points

Combined score


Hematologic score: 3 points

Nonhematologic score: 5 points

Low-intermediate

Risk of severe toxicity

Copy Results 

Next Steps 

Chemotherapy risk
See chemotox table in [Evidence](#) for examples.

0 0

1 +1

2 +2

Hematologic Score

Diastolic blood pressure, mmHg

≤72 mmHg

0

>72 mmHg

+1

Instrumental Activities of Daily Living score (IADL)

26-29 0

10-25 +1

Lactate dehydrogenase, U/L

0-459 U/L

0

>459 U/L

+2

Nonhematologic Score

Eastern Cooperative Oncology Group (ECOG)

6 points

Combined score

Hematologic score: 3 points

Nonhematologic score: 5 points

Low-intermediate

Risk of severe toxicity

Copy Results 📄

Next Steps >>>

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Age at diagnosis



- 70 +

Age must be between 25 and 85

Post Menopausal?



Yes No Unknown

ER status



Positive Negative

HER2/ERBB2 status



Positive Negative Unknown

KI-67 status



Positive Negative Unknown

Positive means more than 10%

Invasive tumour size (mm)



- 36 +

If there was more than one tumour, enter the size of the largest tumour. If neo-adjuvant therapy was undertaken, enter the size before neo-adjuvant therapy.

Tumour grade



1 2 3

Detected by



Screening Symptoms Unknown

Detected as part of a preventive screening programme

Positive nodes



- 1 +

Micrometastases only



Yes No Unknown

"Yes" means the positive node has micrometastases only

Treatment Options

Hormone Therapy



No 5 Years 10 Years

Hormone (endocrine) therapy - using data only from the tamoxifen trials

Available when ER-status is positive

Already received 5 years hormone therapy?



No Yes

Select 'No' only if you are considering therapy options immediately after surgery.

Chemotherapy



None 2nd gen 3rd gen

Trastuzumab



No Yes

Available when HER2/ERRB2 status is positive

Bisphosphonates



No Yes

Available for post-menopausal women

Results

These results may be less accurate for women aged 70 and over

Table

Curves

Chart

Texts

Icons

Select number of years since surgery you wish to consider:

5 10 15

This display shows the number of women who survive at least 10 years after surgery.



- 20 deaths due to other causes
- 15 deaths related to breast cancer
- 3 extra survivors due to bisphosphonates
- 8 extra survivors due to chemotherapy
- 9 extra survivors due to hormone therapy
- 45 survivors with surgery alone

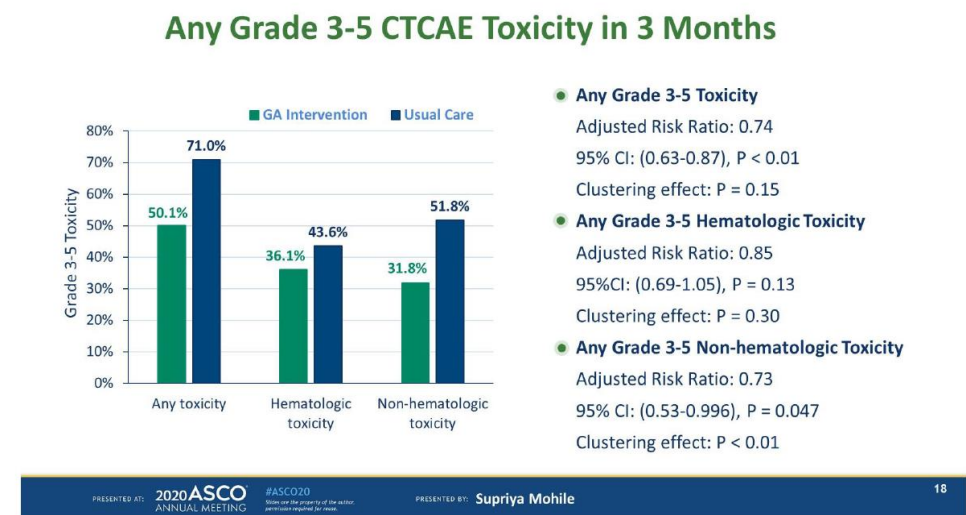
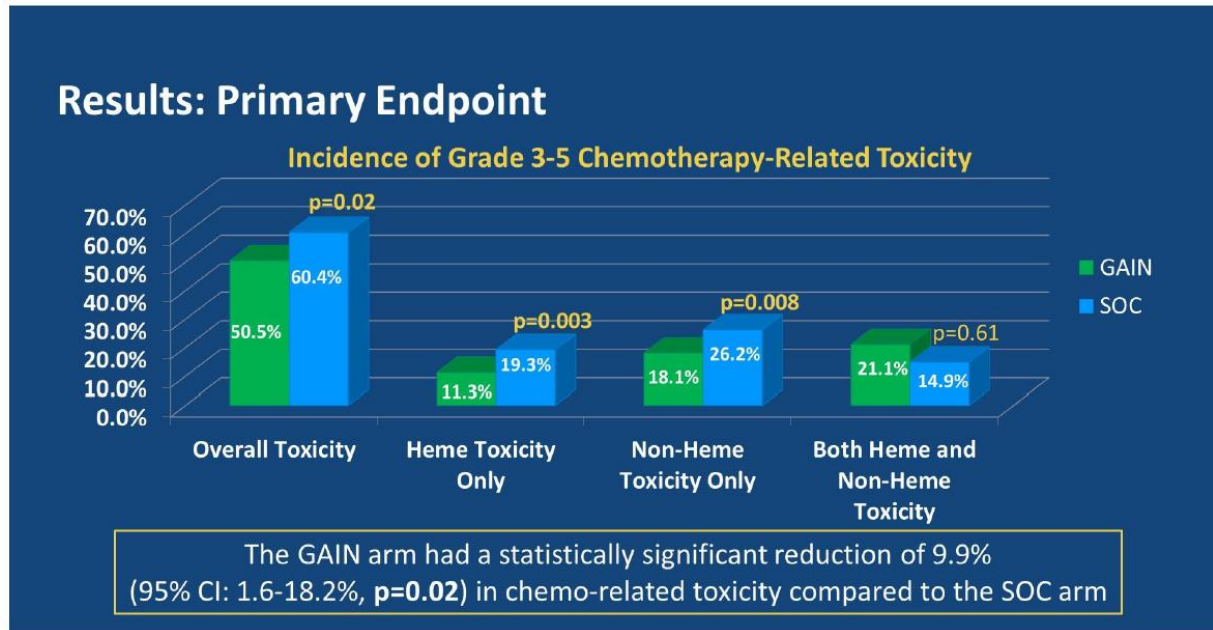
Patient 2: 70 year old woman

- CRASH score ; CARG score
- After discussions with her cardiologist: 6 docetaxel 75-endoxan with GCSF
- Tolerance: asthenia, febrile neutropenia after 1st cure → docetaxel 50
- After 5th cure: acute cardiac failure with LVEF 35% (anemia 9g/dL), with quick recovery. Stop chemotherapy. Radiotherapy. Hormonotherapy.
- 6 months after cancer diagnosis: lives normally. Cured from breast cancer?

CONCLUSION number 1

- Oncologists (and geriatricians)should not be scared using tests!

- A scoring system have to be used only as a tool
- Decisions based on CGA and on clinical experience (Ger-Onc)
- Prediction is important , but prevention is crucial.
- Screening deficiencies (CGA) and making geriatric interventions could decrease the rate of grade 3-5 toxicities: GAIN and GAP 70 studies



Presented By Supriya Mohile at TBD

Vote « **PRO** » (and come and visit us whenever you want)

