



UZ
LEUVEN



The toxicity of targeted agents (in elderly): Implications for care

Hans Wildiers
Medical oncologist, Belgium

Pubmed search

- ‘targeted therapy’ and ‘elderly’



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CRITICAL REVIEWS IN
*Oncology
Hematology*
Incorporating Geriatric Oncology

www.elsevier.com/locate/critrevonc

Targeted anti-cancer therapy in the elderly

Wilson Gonsalves^a, Apar Kishor Ganti^{b,c,*}

^a Department of Internal Medicine, Creighton University Medical Center, Omaha, NE, United States

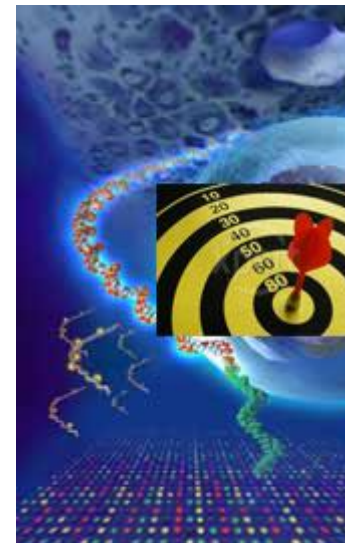
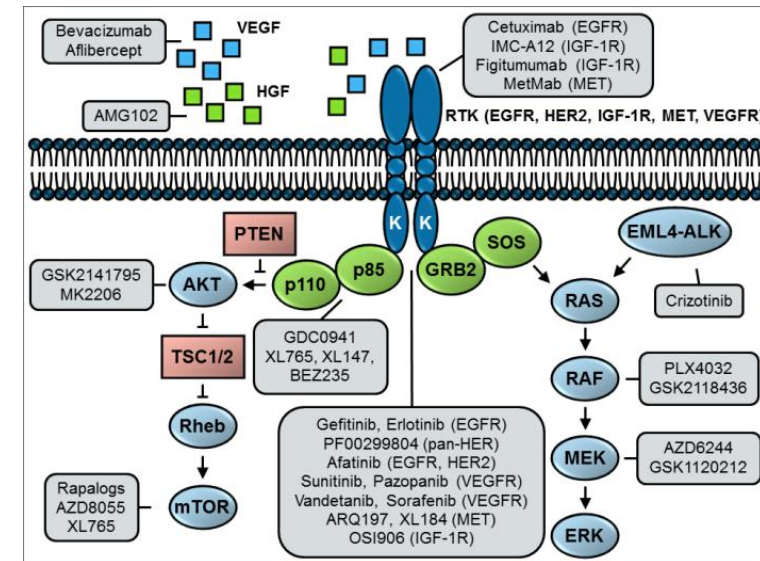
^b Section of Oncology-Hematology, Department of Internal Medicine, VA Medical Center, Omaha, NE, United States

^c Section of Oncology-Hematology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, United States

CHEMOTHERAPY



TARGETED THERAPY



Toxicity

CHEMOTHERAPY

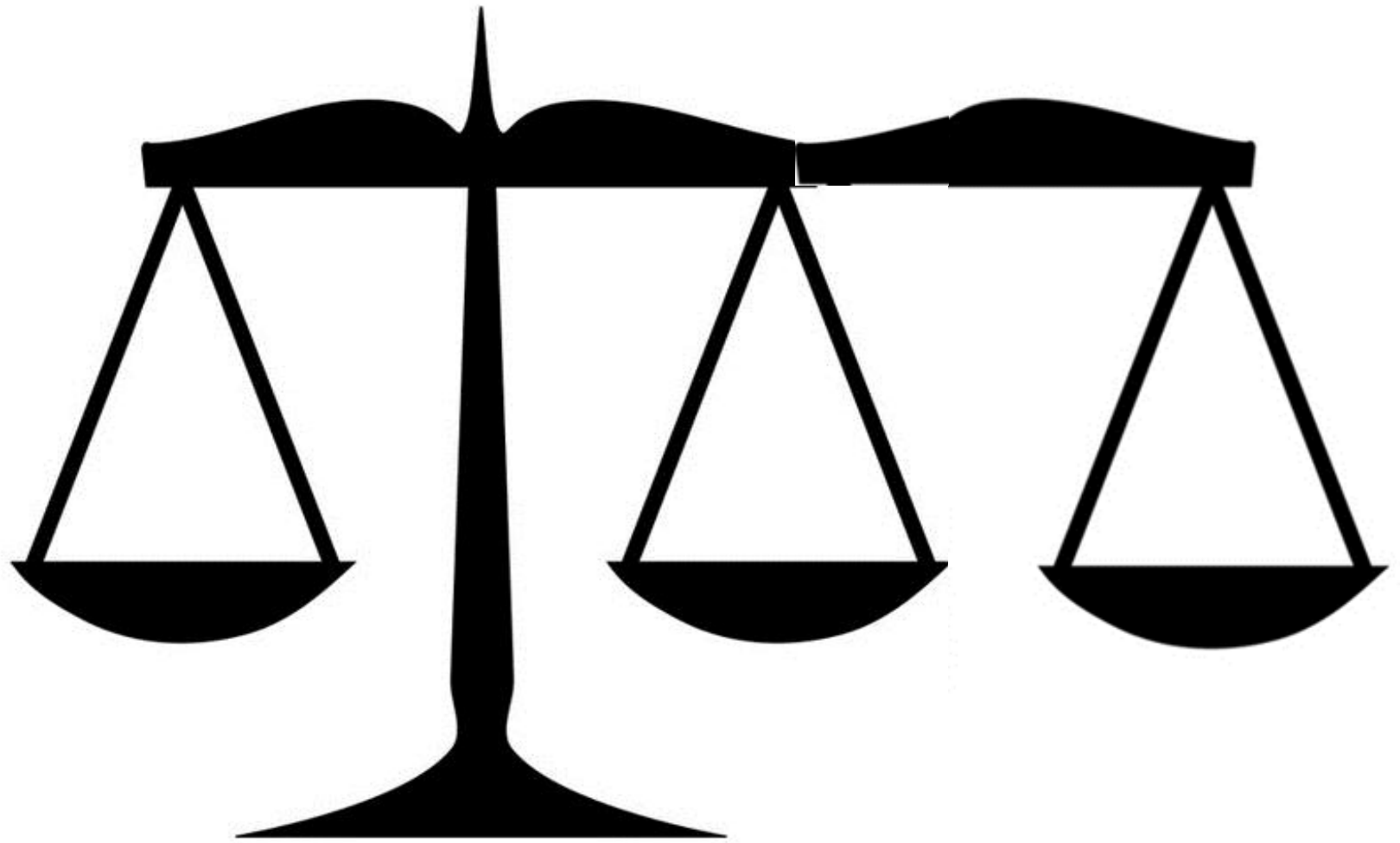
- Myelosuppression
- Alopecia
- Nausea and vomiting
- Neuropathy
- Anorexia
- Mucositis
- Diarrhea
- Fatigue
- Rash
- Cardiac toxicity (cardiac failure)
- Liver dysfunction



TARGETED THERAPY

- \searrow
- \searrow (but hair discoloration, ...)
- \searrow
- \searrow
- =
- =
- =
- = / \nearrow
- = / \nearrow
- = / \nearrow (cardiac failure, aHT)
- = / \nearrow

Targeted agents in metastatic setting



Benefit

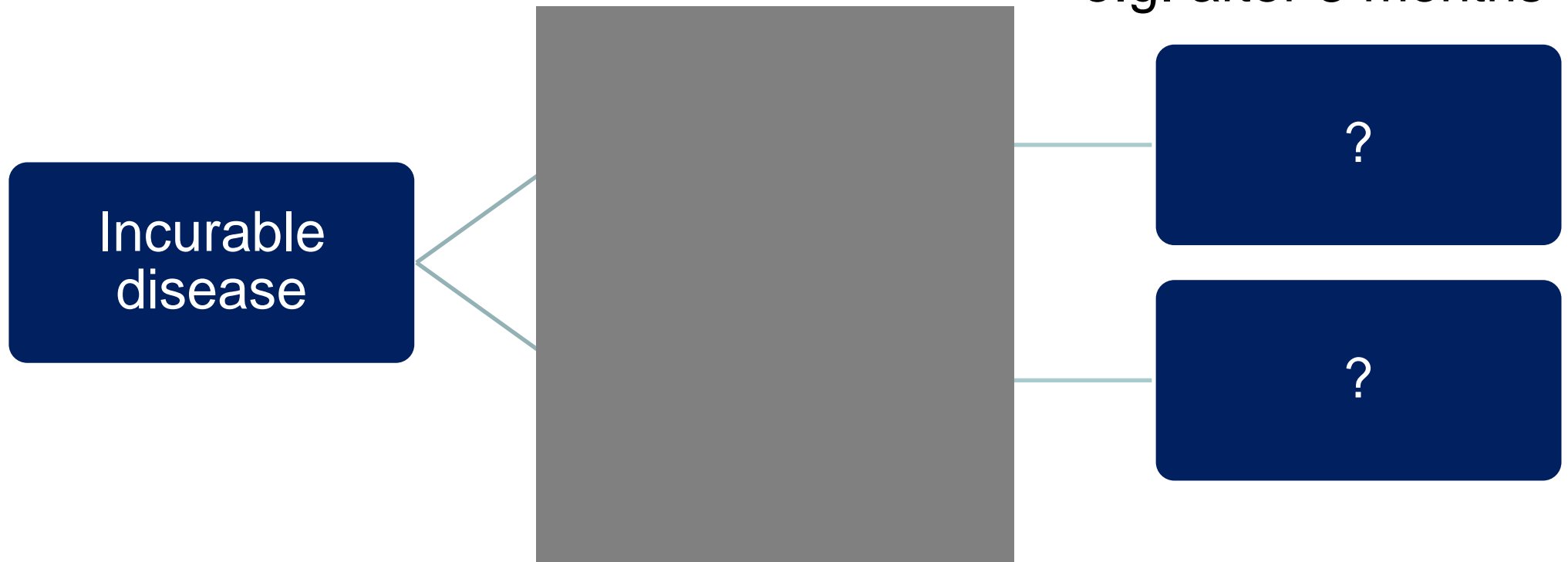
Toxicity

Cost

Goals of treatment?

‘Expensive’ targeted agent

Primary endpoint:
‘**quality of life**’
e.g. after 3 months



Trastuzumab (breast)

BENEFIT

- Major PFS and OS benefit adjuvant and metastatic
- Same benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity =/≠
 - Well tolerated
 - Age = risk factor for cardiac failure (often reversible)

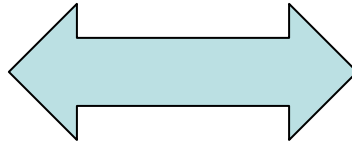
COST

- 18.000 \$ per QALY; cost effective

Lapatinib (breast)

BENEFIT

- TTP 4 → 6 Mo with Xeloda
- Same benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity =
 - rash
 - diarrhea

COST

- 166.000 \$ per QALY; cost effective?

Imatinib (CML, GIST)

BENEFIT

- CML: major OS benefit
- +/- same benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity ↗ ↗ :
 - Gastrointestinal
 - oedema
 - haematological
- Dose intensity ↘: 54%
dose reductions
- Therapy discontinuation due to side effects ↗: 21%

COST

- Probably cost effective (50.000 \$ per QALY)

Erlotinib (NSCLC)

BENEFIT

- OS 5 → 7 Mo in second line
- Same OS benefit in elderly vs younger

COST

- Probably most benefit and cost effective in pts with EGFR mutation!



TOXICITY old vs young

- gr III-IV toxicity ↗: 35% vs 18%
 - Rash: 16% vs 6%
 - Fatigue: 7% vs 2%
 - Stomatitis 3% vs <1%
 - Dehydratation 4% vs <1%
- Dose intensity ↘
- Therapy discontinuation due to side effects ↗: 12% vs 3%
- QoL =
- Toxicity of erlotinib < chemo!

Cetuximab (colon, H&N)

BENEFIT

- Colon:
 - OS 20 → 23,5 Mo in KRAS wildtype
 - Same benefit in elderly vs younger
- H&N:
 - OS 7,4 → 10,1 Mo
 - Worse OS benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity =
 - Rash
 - Diarrhea

COST

- Colon: Probably most beneficial in pts with KRAS wildtype; even there 180.000 \$ per QALY
- H&N: 19.000 \$ per QALY for platinum ineligible pts ; 99.000 \$ per QALY when added to platinum

Sorafenib (HCC, RCC)

BENEFIT

- RCC: PFS 3 → 5,5 Mo
HCC: OS 8 → 11 Mo
- Same benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity ↗: 40% vs 29%
 - Gastrointestinal
 - Fatigue
 - Skin/hand foot syndrome
- Dose intensity ↘: 21 vs 11%
dose reductions
- Therapy discontinuation due to side effects ↗: 21% vs 8%

COST

- RCC/HCC: 75.000 \$ per QALY; cost effective

Sunitinib (RCC, GIST)

BENEFIT

- RCC: OS 21 → 26 Mo compared to IFN α
- Same benefit in elderly vs younger



TOXICITY old vs young

- gr III-IV toxicity =/ \nearrow :
 - Fatigue \nearrow
 - Skin/GI =

COST

- 52.000 \$ per QALY; cost effective

Bevacizumab (...)

BENEFIT

- Breast: 2-5 months PFS benefit, no OS benefit
- NSCLC: OS 10 → 12 Mo
- Colon: OS 16 → 20 Mo
- same or \searrow benefit in elderly vs younger

COST

- Breast: 189.000 \$ per QALY
- NSCLC: 346.000 \$ per QALY
- Colon: 60-80.000 \$ per QALY



TOXICITY old vs young

- gr III-IV toxicity \nearrow (not in all studies)
 - Arterial thrombosis
 - aHT
 - Hemorrhage
 - Febrile neutropenia
 - GI perforation
 - Wound healing problems
 - Toxic deaths mainly > 70y

Cardiac failure and angiogenesis inhibition

- Sorafenib: ?
- Sunitinib: 1,5 -15% clinical heart failure
- Bevacizumab:
 - Rare: 1,6% absolute risk (RRx4)
 - Higher in combination with (after) anthracyclines
 - Age >65y is risk factor
- Often reversible?

Conclusions

Targeted therapy in elderly

- Generally feasible to administer
- Benefit is variable
- Toxicity often (slightly) increased; but often lower than chemotherapy toxicity
- Beware of selection bias: mostly data on 'fit' elderly!
- Balance efficacy – toxicity (- cost) in every individual