

Treatment of castration-resistant prostate cancer (CRPC) in special situations: Treating elderly patients

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Disclosures

□ Pr Stéphane Oudard has consulting agreements with:

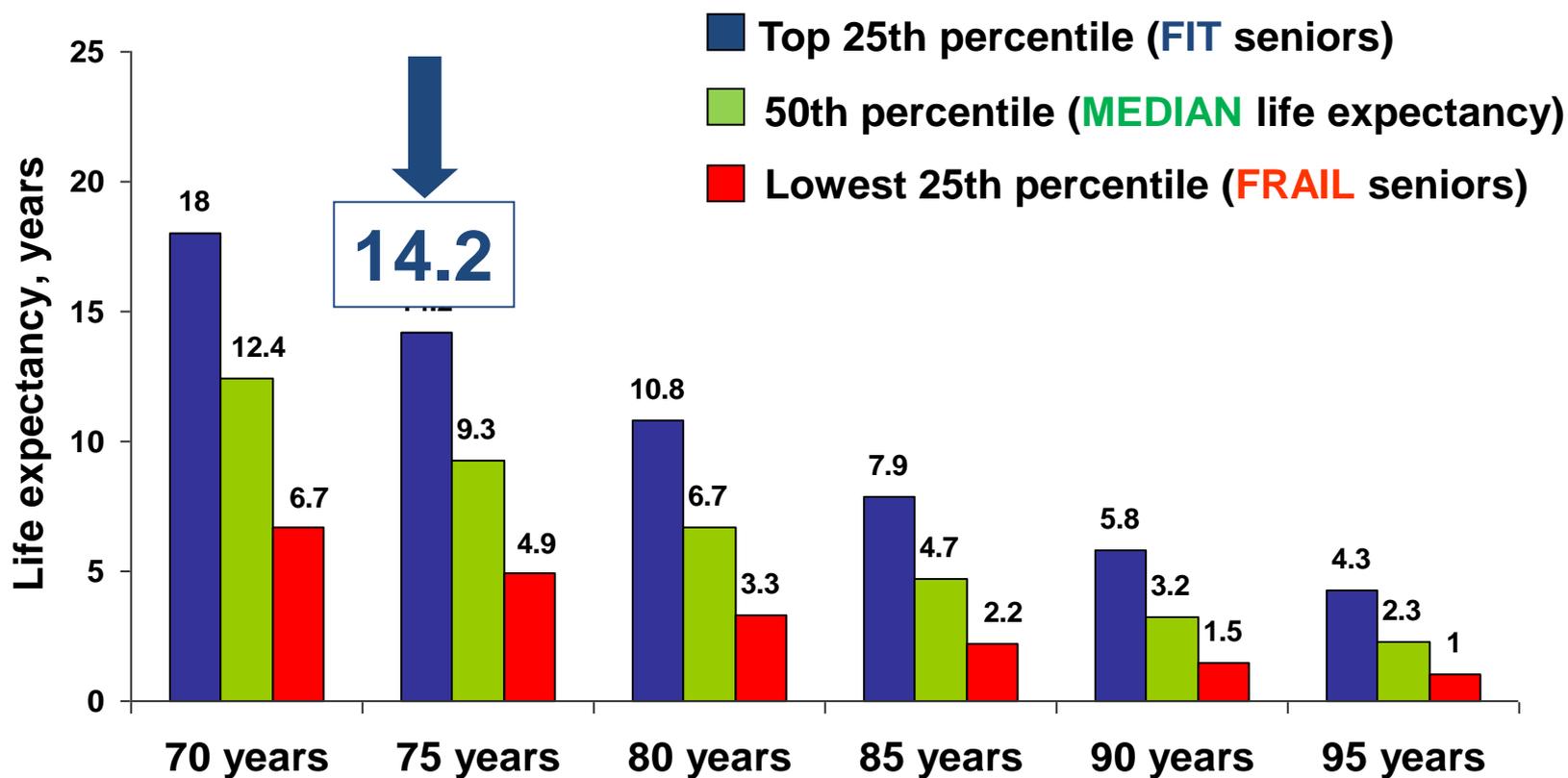
- Bayer
- Janssens
- Astellas
- Dendreon
- Sanofi
- Takeda
- Ipsen
- Amgen

Clinical case of one patient from my institution

- NOR-B, A 75-year old, living in Paris
- Complains of nocturia (5-6/night)
- PSA: 250 ng/ml
- Prostate biopsy: 8/12 positive cores, Gleason 8 (4+4)
- Bone scan: multiple mets
- CT scan: pelvic lymph nodes
- General condition:
 - Married (wife 65-year old), 2 children
 - Leads an active life...cyclist and plays golf
 - Comorbidity: uncontrolled hypertension

If this man had no
metastatic prostate cancer,
what would be his life expectancy?

Life Expectancy in Senior Adults



75-year old, Gleason 8, short response to first ADT (12 months), multiple bone mets, mCRPC

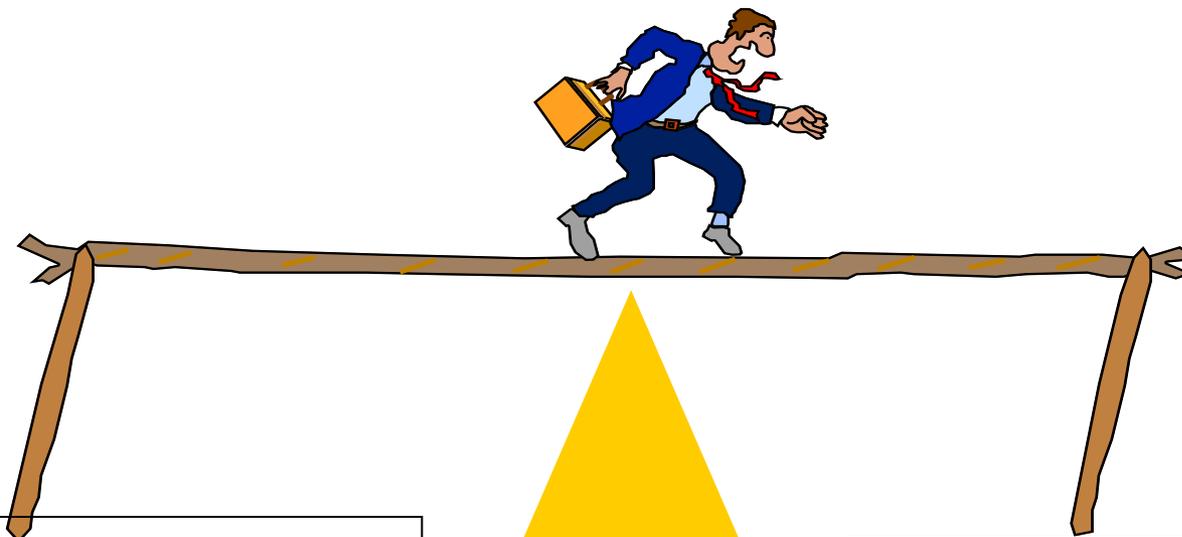
What would you recommend to this patient?

1. Try a new AR-targeted agent because the patient is too old for chemotherapy
2. Chemotherapy + prophylactic G-CSF
3. Radium 223
4. Need for further geriatric evaluation to decide

Clinical case of one patient from my institution

- NOR-B, A 75-year old, living in Paris
- PSA: 249 ng/ml, Gleason 8 (4+4)
- Multiple bone mets and pelvic lymph nodes
- General condition:
 - Married (wife 65-year old), 2 children
 - Leads an active life...cyclist and plays golf
 - Comorbidity: **uncontrolled hypertension**
 - **No malnutrition, no loss of weight**
 - **No cognitive impairment**
 - **Independent in activities of daily living**
 - **Questionnaire G-8: 14 points**

Need of an accurate risk evaluation



Risk of death due to prostate cancer
⇒ aggressiveness of the tumor

Risk of death due to other cause
⇒ Health status+++

Management of prostate cancer in older patients: updated recommendations of a working group of the International Society of Geriatric Oncology

Jean-Pierre Droz, Matti Aapro, Lodovico Balducci, Helen Boyle, Thomas Van den Broeck, Paul Cathcart, Louise Dickinson, Eleni Efstathiou, Mark Emberton, John M Fitzpatrick, Axel Heidenreich, Simon Hughes, Steven Joniau, Michael Kattan, Nicolas Mottet, Stéphane Oudard, Heather Payne, Fred Saad, Toru Sugihara*

In 2010, the International Society of Geriatric Oncology (SIOG) developed treatment guidelines for men with prostate cancer who are older than 70 years old. In 2013, a new multidisciplinary SIOG working group was formed to update these recommendations. The consensus of the task force is that older men with prostate cancer should be managed according to their individual health status, not according to age. On the basis of a validated rapid health status screening instrument and simple assessment, the task force recommends that patients are classed into three groups for treatment: healthy or fit patients who should have the same treatment options as younger patients; vulnerable patients with reversible impairment who should receive standard treatment after medical intervention; and frail patients with non-reversible impairment who should receive adapted treatment.

Lancet Oncol 2014; 15: e404-14

SIOG recommendations for senior men

Treatment recommendations for older men
with prostate cancer should be based on:

Health status

(driven by co-morbidities, dependence and nutritional status)

AND

Patient preferences

NOT chronological age

Comorbidities: Cumulative Illness Score Rating-for Geriatrics (CISR-G)

Heart	Total number of categories endorsed
Vascular	
Hematopoietic	Total Score
Respiratory	
Eyes, Ears, Nose, Throat & Larynx	Severity index (total score / total number of categories endorsed)
Upper GI	
Lower GI	Number of categories at level 3 severity
Liver	
Renal	Number of categories at level 4 severity
Genitourinary	
Musculoskeletal/Integument	
Neurological	
Endocrine/Metabolic & Breast	
Psychiatric Illness	

RATING STRATEGY: 0= no problem; 1= Current mild problem or past significant problem; 2= Moderate disability or morbidity/ requires "first line" therapy; **3= Severe/constant significant disability/uncontrollable chronic problems; 4= Extremely severe/immediate treatment required/end organ failure/severe impairment in function**

Health status evaluation: Activities Daily Living (ADL) and Instrumental ADL (IADL) in senior adults

Activity (ADL)
Bathing
Dressing
Going to toilets
Moving out of bed or chair
(Continence)
Feeding

Activity (IADL)
Take own medication without help
Manage money without help
Use telephone without help
Go to places out of walking distance without help

One abnormality is significant

¹IADL: simplified Instrumental Activities of Daily Living (Lawton, Gerontologist 1969, 9: 179)

²ADL: index of independence in Activities of Daily Living (Katz, JAMA 1963, 185: 914)

Other components of health status

Nutritional status

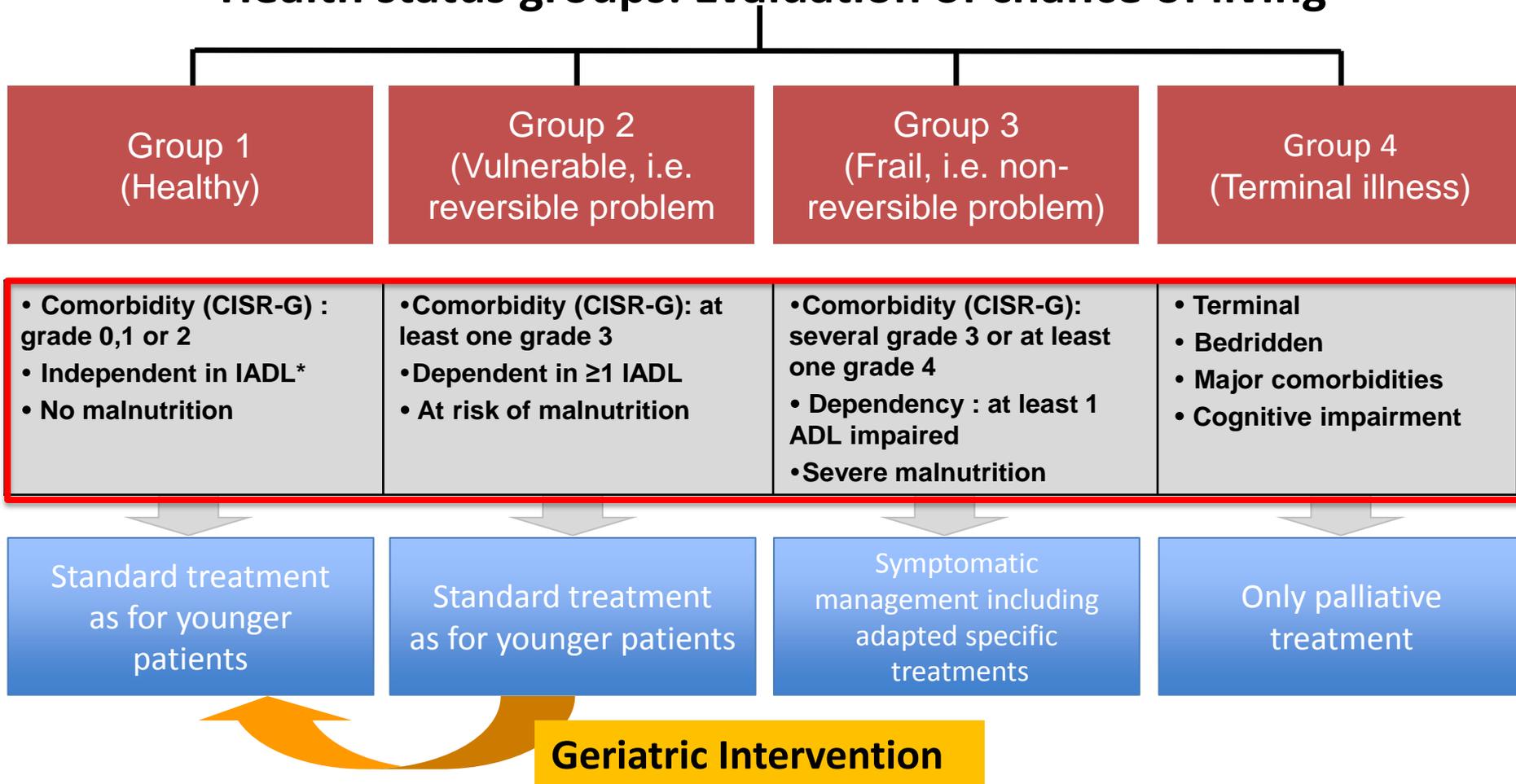
- No weight loss (<5% body weight within last 3 months)
- Moderate malnutrition (weight loss of 5-10%)
- Severe malnutrition (weight loss \geq 10%)

(Mental Health)

- Cognitive impairment

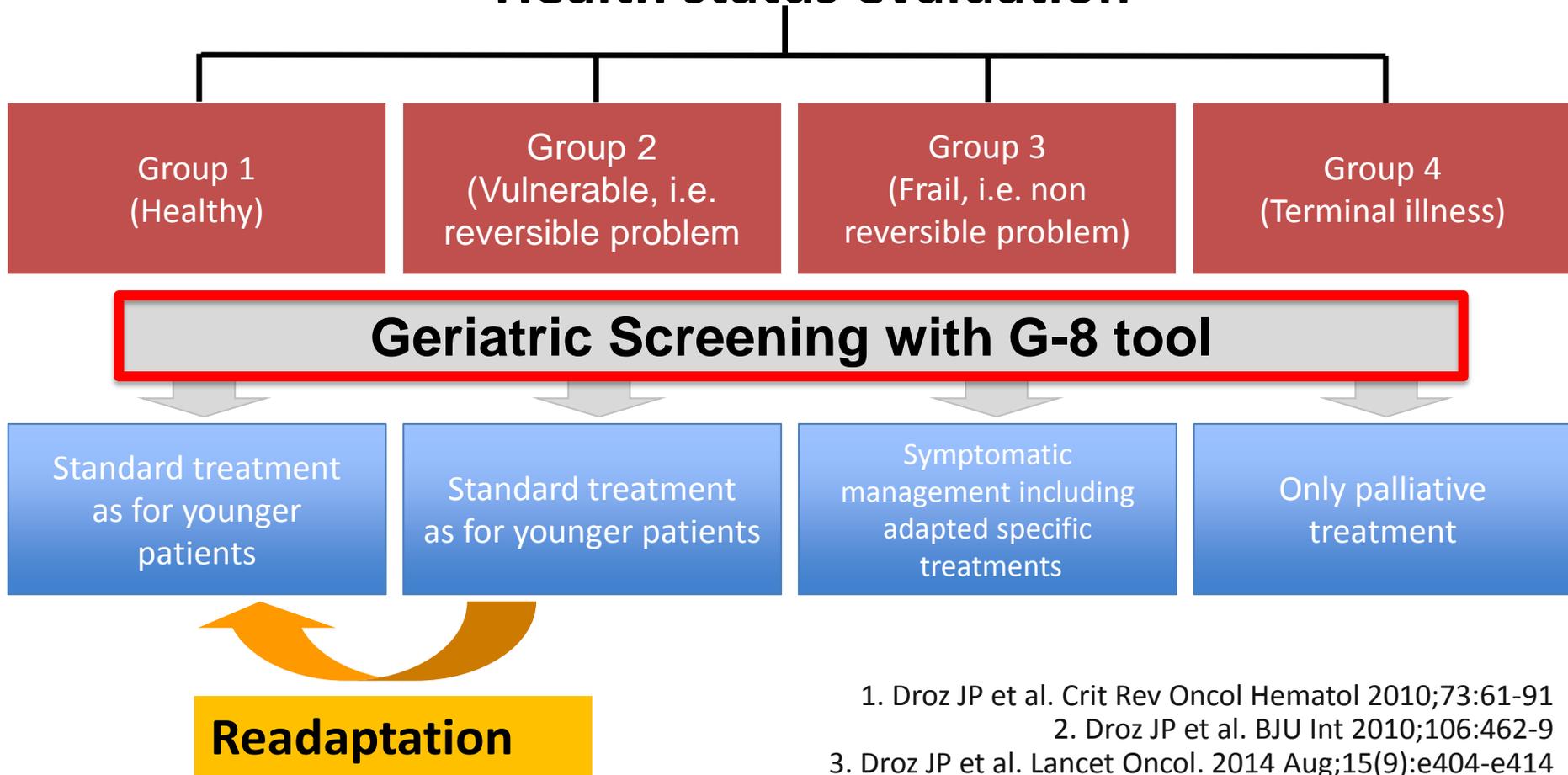
SIOG classification of Health Status 2010

Health status groups: Evaluation of chance of living



Principles of 2014 SIOG guideline

Health status evaluation



1. Droz JP et al. Crit Rev Oncol Hematol 2010;73:61-91
2. Droz JP et al. BJU Int 2010;106:462-9
3. Droz JP et al. Lancet Oncol. 2014 Aug;15(9):e404-e414

ONCODAGE – G8

Items	Score for possible responses	
A	Has food intake declined over the past 3 months owing to loss of appetite, digestive problems, difficulties with chewing or swallowing?	0=severe decrease in food intake 1=moderate decrease in food intake 2=no decrease in food intake
B	Weight loss during the past 3 months	0=weight loss of more than 3 kg 1=does not know 2=weight loss between 1 kg and 3 kg 3=no weight loss
C	Mobility	0=bed or chair bound 1=able to get out of bed or chair but does not go out 2=goes out
E	Neuropsychological problems	0=severe dementia or depression 1=mild dementia 2=no psychological problems
F	Body-mass index	0=<19.0 kg/m ² 1=19.0-20.9 kg/m ² 2=21.0-22.9 kg/m ² 3>=23.0 kg/m ²
G	Does the patient take more than three prescribed drugs per day?	0=yes 1=no
H	By comparison with other people of the same age, how does the patient consider his health status?	0=not as good 0-5=does not know 1-0=as good 2-0=better
I	Age	0=>85 years 1=80-85 years 2=<80 years
Total score	0-17	

Adapted from Bellera and colleagues¹¹ by permission of Oxford University Press.

Table 1: G8 geriatric assessment instrument to determine baseline characteristics

- Cut-off : Abnormal if ≤ 14 .
- Sensibility: 76.6%
- Specificity : 64.4%
- Reproducibility: kappa: 0.65

- **Duration of the test:**
4.4 minutes

<http://espacecancer.sante-ra.fr/oncogeriatric/default.aspx>

ONCODAGE – G8

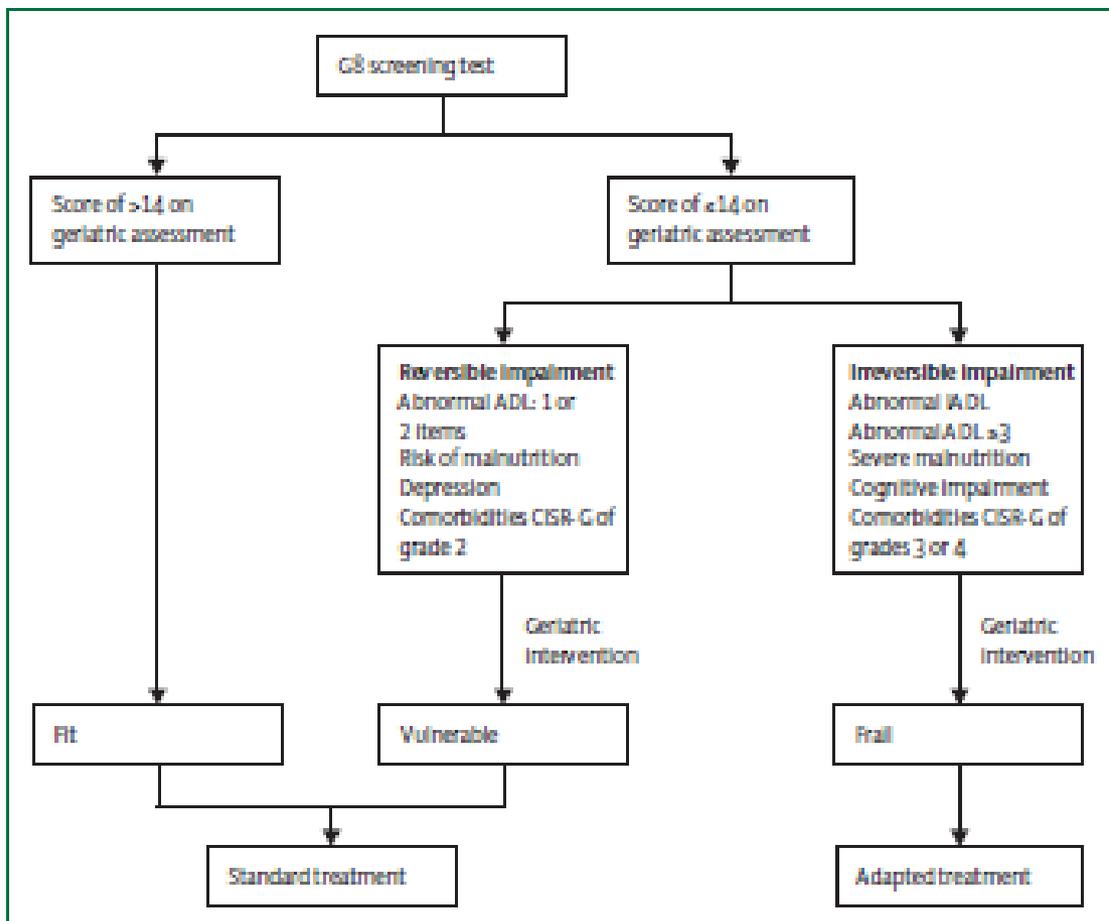


Figure 2: Decision tree for treatment of prostate cancer according to health status assessment
 ADL=Activities of Daily Living. IADL=Instrumental Activities of Daily Living. CISR-G=Cumulative Illness Score Rating-Geriatrics.

ONCODAGE – G8 impact on OS

Diagnostic characteristics of the G8 geriatric screening tool to identify patients with a geriatric risk profile and to evaluate their prognostic value for functional decline and overall survival

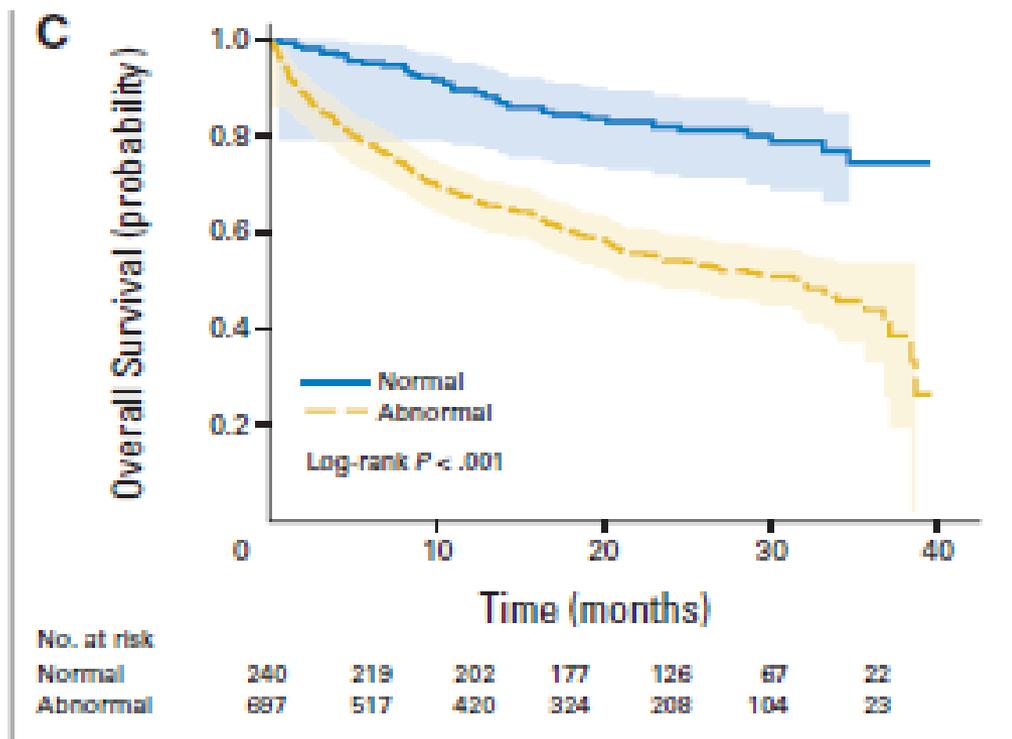


Fig 2. Prognostic value for overall survival of the Flemish version of the Triage Risk Screening Tool (tTRST), including tTRST (1), tTRST (2), and G8 (N = 937). Product-limit survival estimates with No. of patients at risk and 95% Hall-Wellner bands. (A) tTRST (1). (B) tTRST (2). (C) G8.

Management of metastatic CRPC:

Specific considerations for senior adults

➤ Castration-resistant metastatic prostate cancer (mCRPC)

- Docetaxel
 - 3-weekly schedule is the standard of care ^{1,2}
 - Weekly or Bi-weekly schedule for frail patients ³⁻⁴
- Cabazitaxel ^{5,6}
- Abiraterone acetate ^{7,8}
- Enzalutamide ^{9,10}
- Sipuleucel-T ^{11,12}

➤ Palliative therapy for bone metastases

- Zoledronic acid and Denosumab ^{13,14}

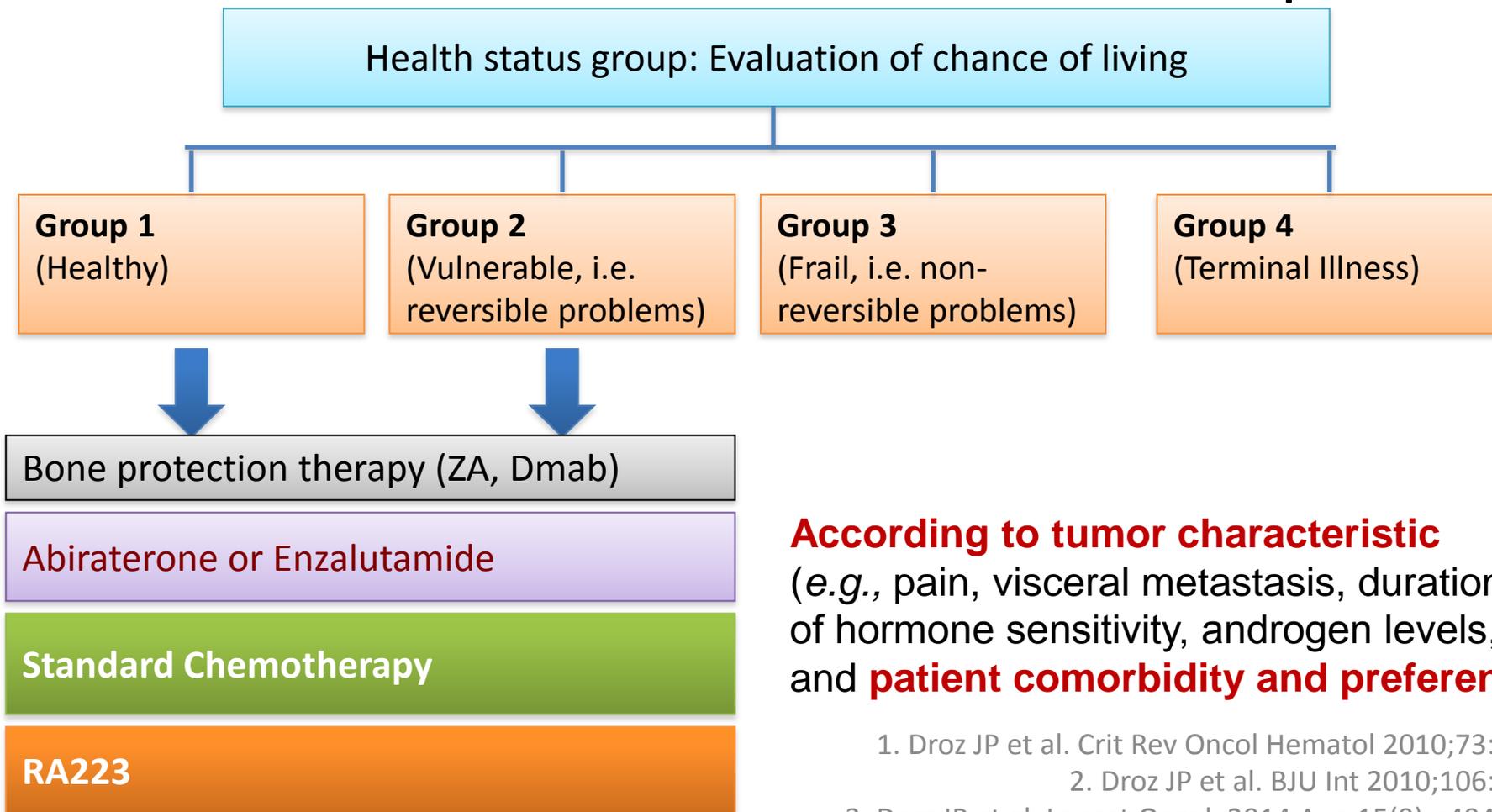
1. Tannock I et al, N Engl J Med 2004; 351: 1502-12 ; 2. Berthold D et al. J Clin Oncol 2008;26:242-5 ; 3. Fossa S et al. Eur Urol 2007;52:1691-9; 4. Kellokumpu-Lehtinen P et al. Lancet Oncol 2013;14:117-124 ; 5. De Bono J et al, Lancet 2010; 376:1147-54 ; 6. Bahl A et al, Ann Oncol 2013; 24: 2402-08 ; 7. De Bono J et al, N Engl J Med 2011; 364: 1995-2005 ; 8. Fizazi K et al, Lancet Oncol 2012; 13: 983-92 ; 9. Scher H et al, N Engl J Med 2012; 367: 1187-97 ; 10. Beer T et al, N Engl J Med. 2014 Jul 31;371(5):424-33 ; 11. Kantoff P et al, N Engl J Med 2010; 363: 411-22 ; Small E et al, J Clin Oncol 24:3089-3094 ; 13. Saad F et al, J Natl Cancer Inst 2004; 96: 879-82 ; 14. Fizazi K et al, Lancet 2011; 377: 813-22

Effect of age on efficacy for the different treatments in mCRPC: No difference

Age (Years)	Study and drugs (HR: 95%)				
	TAX327 ^{1,2} (Docetaxel)	TROPIC ³ (Cabazitaxel)	COU-301 ⁴ (Abiraterone)	AFFIRM ⁵ (Enzalutamide)	Sipuleucel-T ⁶
< 65	0.7 (0.xx-0.xx)	0.81 (0.61-1.08)	0.69 (0.53-0.91)	0.63 (0.46-0.87)	/
≥ 65	0.82 (0.xx-0.xx)	0.62 (0.50-0.78)	0.76 (0.63-0.90)	0.63 (0.51-0.78)	0.5
≥ 75	0.74 (0.xx-0.xx)	/	0.64 (0.48-0.85)	/	0.6

1. Tannock I et al, N Engl J Med 2004; 351: 1502-12 ; 2. Berthold D et al. J Clin Oncol 2008;26:242-5 ; 3. De Bono J et al, Lancet 2010; 376:1147-54 ; 4. De Bono J et al, N Engl J Med 2011; 364: 1995-2005 ; 5. Scher H et al, N Engl J Med 2012; 367: 1187-97 ; 6. Kantoff P et al, N Engl J Med 2010; 363: 411-22

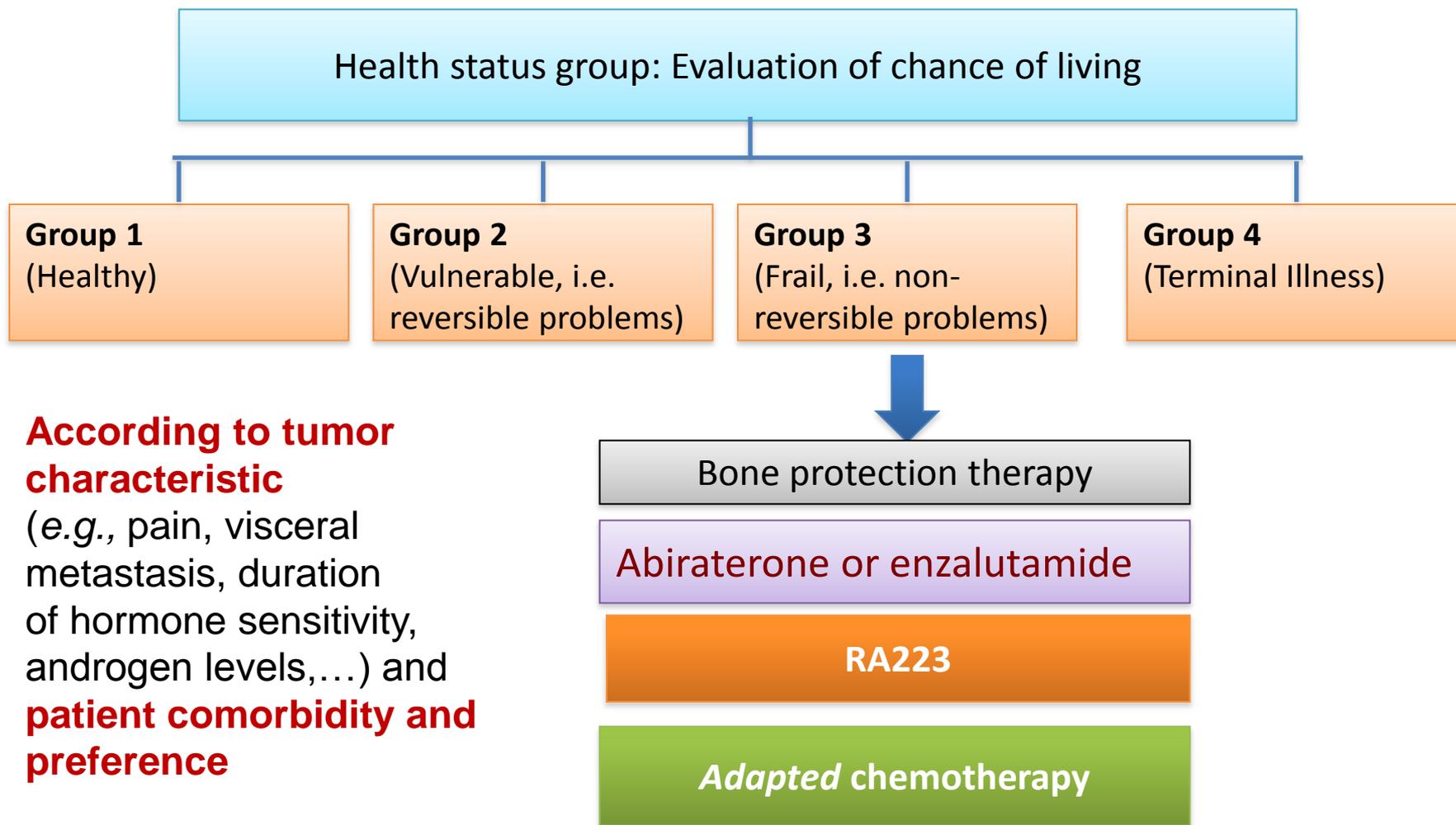
mCRPC treatment strategy, in the current landscape



According to tumor characteristic (e.g., pain, visceral metastasis, duration of hormone sensitivity, androgen levels,...) and **patient comorbidity and preference**

1. Droz JP et al. Crit Rev Oncol Hematol 2010;73:61-91
2. Droz JP et al. BJU Int 2010;106:462-9
3. Droz JP et al. Lancet Oncol. 2014 Aug;15(9):e404-e414

Treatment strategy, in the current landscape



According to tumor characteristic
(e.g., pain, visceral metastasis, duration of hormone sensitivity, androgen levels,...) and **patient comorbidity and preference**

Adapted weekly Cabazitaxel (10 mg/m²) after progression on docetaxel in elderly patients in mCRPC

Patient characteristics

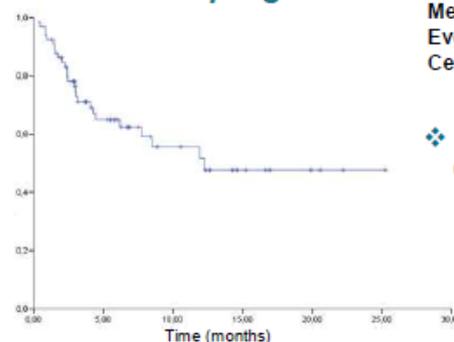
Patient characteristics	
Evaluable patients	66
Age (years)	
Mean (SD)	72,5 (7,1)
Median	73,3
Range	54,6 - 84,9
ECOG n(%)	
0	8 (12,1)
1	13 (19,7)
2	44 (66,7)
UK	1 (1,5)
Charlson score	
Median	6,0
Unit criteria	
ECOG 2	47 71,2
Dose reduction due to FN	10 15,2
RT affecting more than 25% of bone marrow	8 12,1
Metastasis	
Bone	55 45,8
Lymphatic nodes	16 34,0
Liver	9 7,5
Lung	7 10,6
Adrenal glands	3 2,5
Pleura	1 2,1

Treatment-related adverse events

Most frequent toxicity per patient	Grade I		Grade II		Grade III		Grade IV	
	N	%	N	%	N	%	N	%
Anemia	25	37,9	18	27,3	3	4,5	1	1,5
Leucopenia	11	16,7	5	7,6	-	-	-	-
Neutropenia	4	6,1	2	3,0	1	1,5	1	1,5
Thrombocytopenia	6	9,1	1	1,5	3	4,5	-	-
Asthenia	12	18,2	10	15,2	7	10,6	-	-
Diarrhea	13	19,7	4	6,1	1	1,5	-	-
Nausea	8	12,1	3	4,5	1	1,5	-	-
Anorexia	7	10,6	4	6,1	1	1,5	-	-
Vomiting	6	9,1	-	-	1	1,5	-	-
Neuropathy	1	1,5	1	1,5	-	-	-	-
General deterioration	-	-	-	-	1	1,5	-	-

Eight patients discontinued the study due to asthenia G3 (5), mucositis G3 (1), cardiac toxicity (1) and general deterioration (1). No febrile neutropenia was reported.

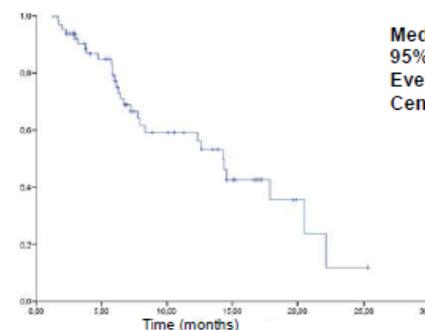
Time to PSA progression



Median (months): 12,3
Events: 26
Censored: 40

❖ PFS at 12 weeks: 74,6%
(95% CI: 63,8 – 85,4)

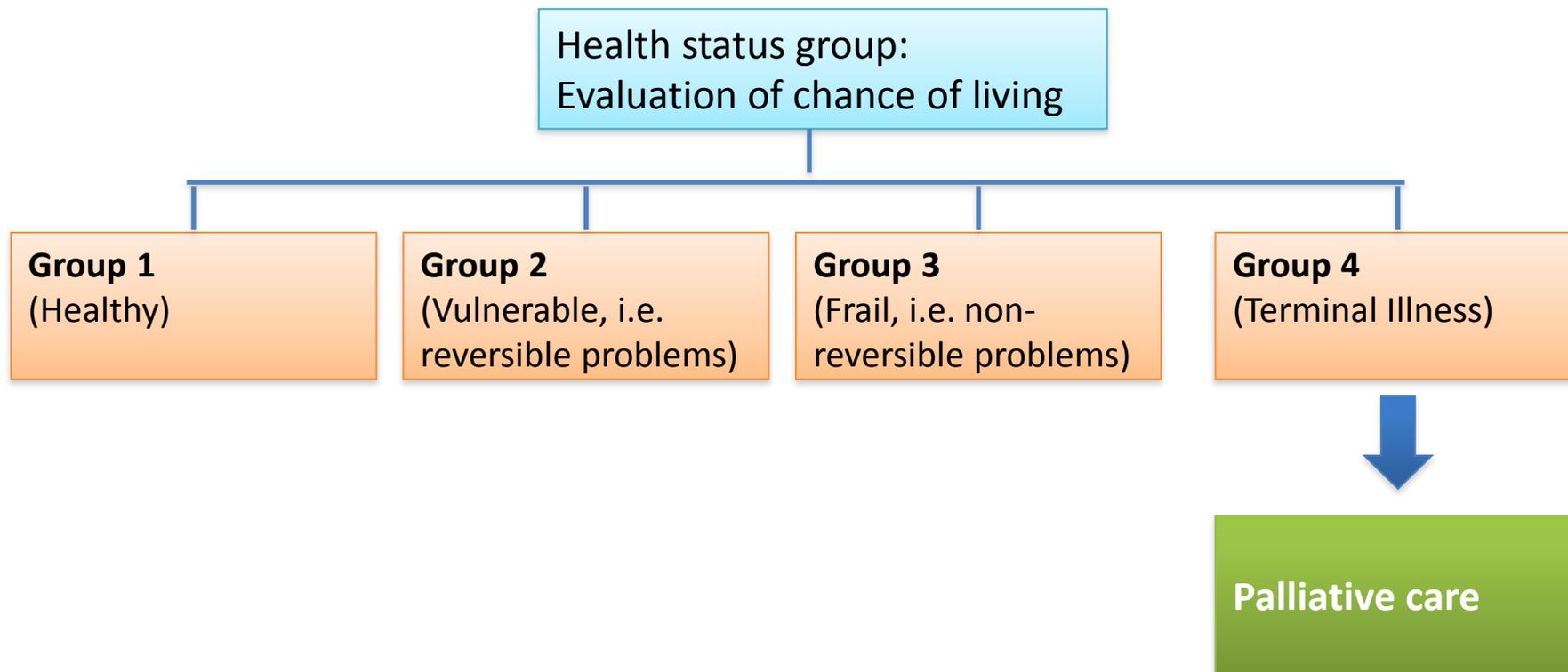
Overall survival



Median (months): 14,3
95% CI: 11,8-16,8
Events: 29
Censored: 37

B. Perez-Valderrama et al, SOGUG study ESMO 2014

Treatment strategy, in the current landscape



Adapted from Droz JP et al, *Crit Rev Oncol Hematol.* 2010, 73: 61-91;
Droz JP et al. *BJU Int.* BJU Int. 2010 Aug;106(4):462-9 and EAU guidelines

Take Home Messages

- PCa in senior adults is a public health problem
- The critical issue in decision making process is the competition between the risk of death due to PCa and the risk of death due to health status worsening
- Efficacy of PCa treatments for advanced disease is similar in younger and older patients
- Treatment choice should be based on tumor and patient characteristics
- **Health status can be easily evaluated by G-8 questionnaire**