



- 1. How to treat (or not) elderly colorectal cancer patients**
- 2. Unfit: a relative concept**

**by Ass. Prof. Fotios Loupakis, Prof. Hans Prenen
and Ass. Prof. Joleen Hubbard**

HOW TO TREAT (OR NOT) ELDERLY COLORECTAL CANCER PATIENTS

by Ass. Prof. Fotios Loupakis
Azienda Ospedaliero-Universitaria Pisana
Pisa, Italy

ELDERLY: A SUBGROUP?

Bowel cancer incidence statistics

Cases



New cases of
bowel cancer,
2013, UK

Proportion of all cases



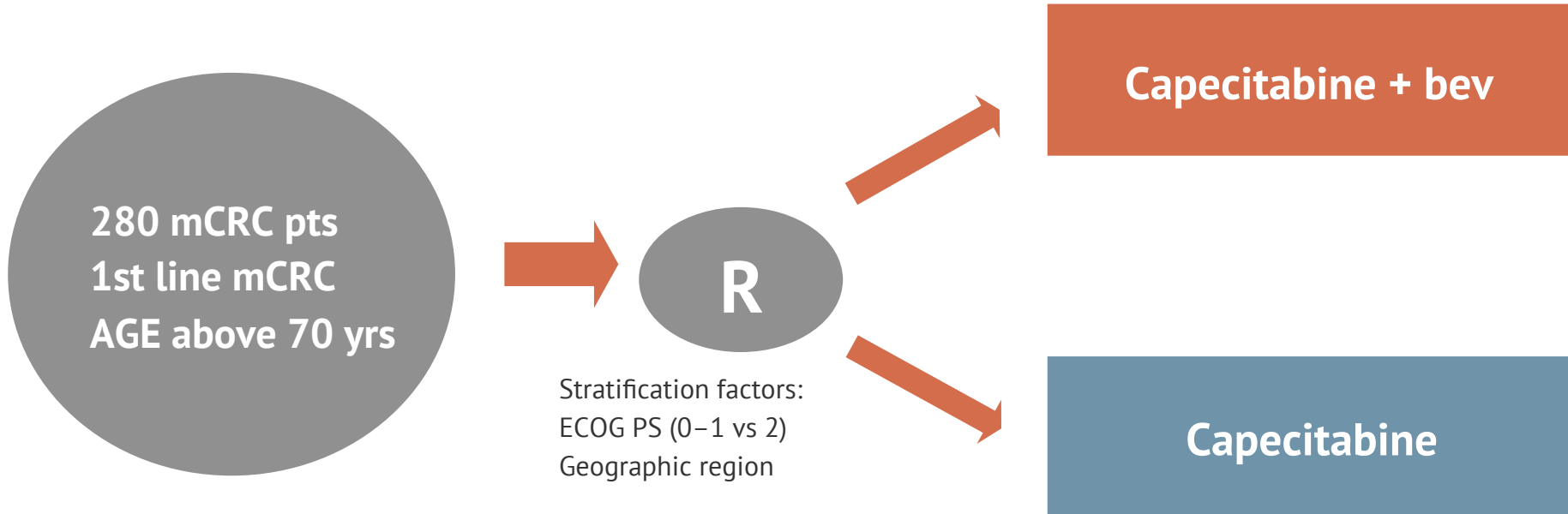
Percentage
bowel cancer is
of total cancer
cases, 2013,
UK

Age



Age that almost
6 in 10 of bowel
cancer cases
are diagnosed,
2011-2013, UK

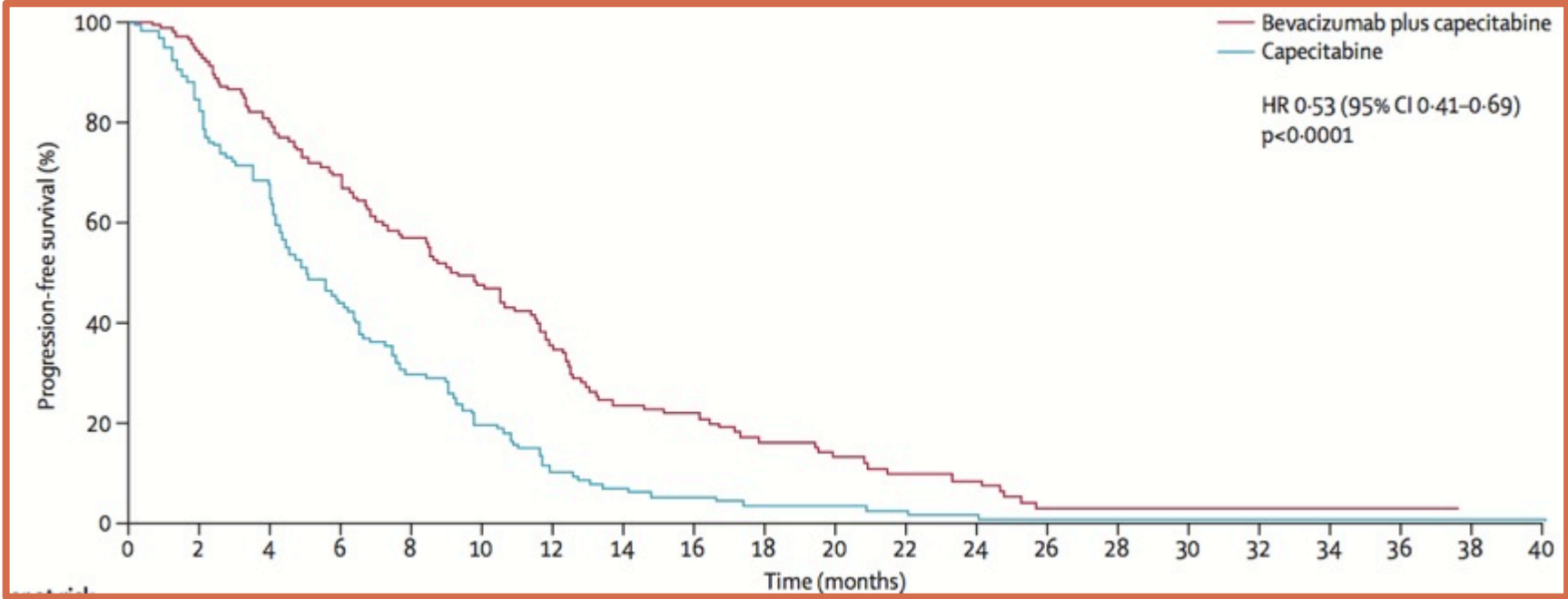
THE AVEX STUDY



Key inclusion criteria

- ECOG PS 0-2
- Prior adjuvant chemotherapy allowed if completed >6 month before inclusion
- Not optimal candidates for a combination chemotherapy with irinotecan or oxaliplatin

AVEX - PROGRESSION FREE SURVIVAL



nature
REVIEWS

CLINICAL ONCOLOGY



LIQUID BIOPSY

Tracking tumour evolution to enable dynamic adaptation of therapy

First-line chemotherapy for metastatic CRC
Review and evidence-based algorithm

PERSPECTIVES

First-line chemotherapy for mCRC — a review and evidence-based algorithm

Roberto M. Cremolini, Marta Schirripa, Carlotta Antoniotti, Roberto Moretto, Alfredo Salvatore, Gianluca Masi, Alfredo Falcone and Fotios Loupakis

Abstract | The response to first-line therapy is a primary determinant of outcome in patients with metastatic colorectal cancer (mCRC), for three main reasons: effective first-line therapy provides a unique opportunity to cure some patients; can be crucial in preventing disease progression and achieving symptom relief; and can improve patient quality of life. The choice of first-line therapy is a complex decision, with many factors influencing the choice of first-line therapy for, and the effectiveness of, further treatments. In the past decade, decision-making regarding the choice of first-line therapy for mCRC has been complicated by the availability of many different options without a definitive consensus on a specific standard of care (despite major advances in categorizing predictive molecular disease subtypes). Most of the efforts of the scientific community have been directed at establishing the best biologic agent to be combined with a chemotherapy doublet, through a different branch of research has produced new data that underscore the importance of defining the optimal chemotherapy backbone. Herein, we review the clinical trials completed in the past 10 years that have investigated and compared the use of chemotherapy doublets, triplets, and monotherapies, with or without molecularly targeted biologic agents, in the first-line treatment of patients with mCRC. Our examination of the literature led us to propose a new patient-oriented algorithm to guide clinicians' decisions on the best choice of upfront therapy for mCRC.

Introduction

Colorectal cancer (CRC) is the second most frequent cause of cancer-related death in Europe and in the USA.^{1,2} Around 50% of patients with CRC present with metastases at the time of diagnosis and over 25% will subsequently develop distant recurrences.^{3,4} The median overall survival for patients affected by metastatic colorectal cancer (mCRC) has notably increased in the past 20 years, from 12 months in the 1970s to 20 months in the 2000s, and to 18 months in which 5-fluorouracil (5-FU)-based chemotherapy was the standard of care.⁵ In 2014, the standard of care for first-line mCRC was published in 2014.^{6,7}

Selection of the optimal first-line treatment forms a crucial foundation of the therapeutic pathway for patients with mCRC. The strategic value of this choice lies in the importance of achieving disease control to enable subsequent interventions, in terms of surgical and/or locoregional approaches, and other systemic treatments. In the past few years, many drug combinations have emerged as possible options for first-line therapy and the selection of the most appropriate regimen represents a challenging issue for medical oncologists.

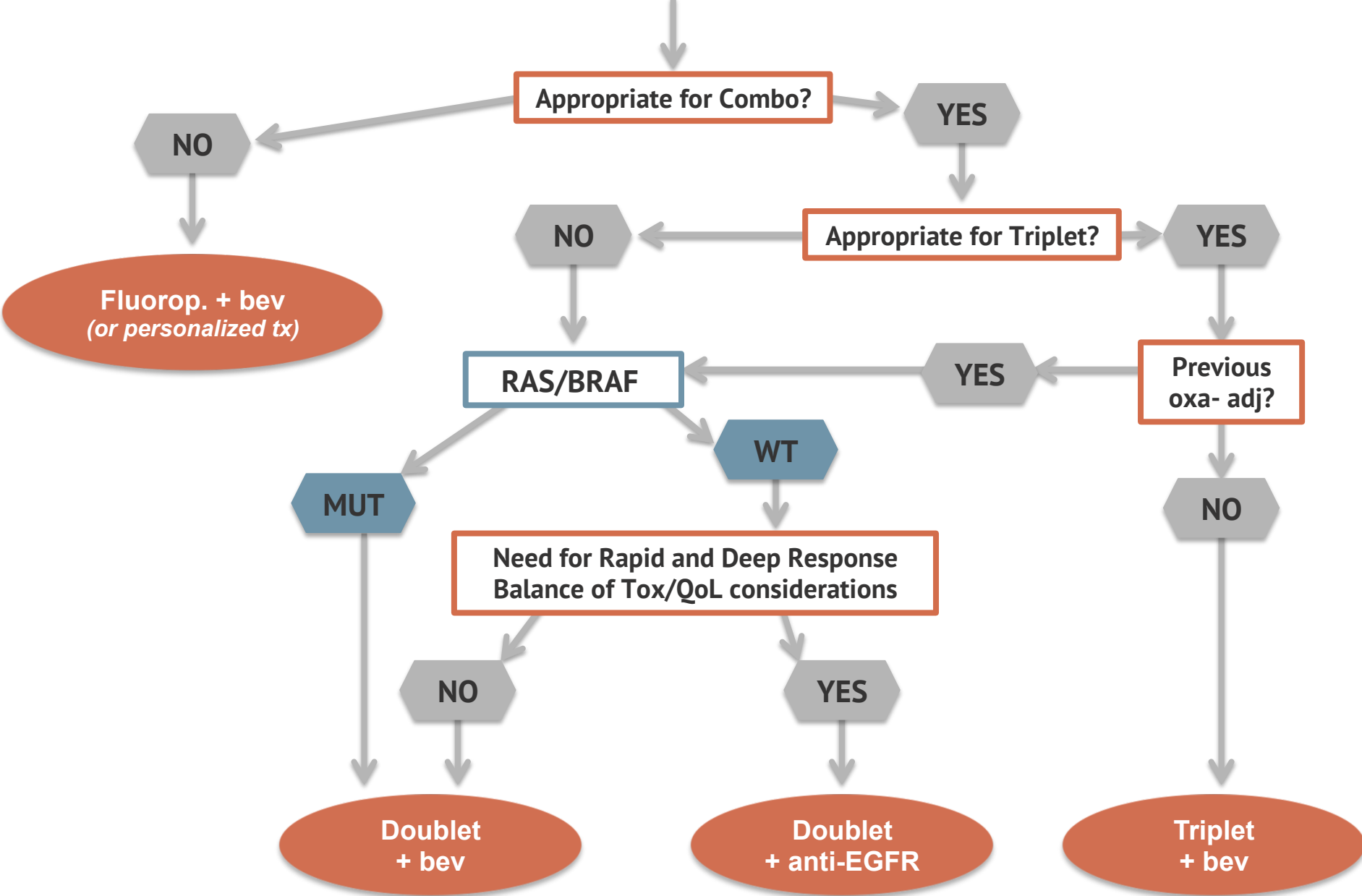
The introduction of oxaliplatin and irinotecan into the clinical practice, and the demonstration of their efficacy and the

in the development of the triplet chemotherapy regimen of the triplet chemotherapy regimen FOLFOXIRI comprising these three cytotoxic drugs and folinic acid. This triplet was demonstrated to have greater antitumour activity and therapeutic efficacy than FOLFIRI in a phase III randomized trial.⁸ During the same years, the therapeutic armamentarium available for the first-line treatment of mCRC was enriched by the introduction of molecularly targeted biologic agents: the anti-VEGF monoclonal antibody (mAb) bevacizumab,⁹ and the anti-EGFR mAbs cetuximab¹⁰ and panitumumab.¹¹

Since the introduction of these molecularly targeted agents, research efforts have been focused on the choice of the 'best biologic agent' for the treatment of patients with mCRC. The relatively recent recognition of the negative predictive value of mutations in the RAS genes (specifically KRAS and NRAS) with regard to the efficacy of anti-EGFR mAbs led to the exclusion of this class of drugs in only a subset of patients with RAS-wild-type mCRC. In fact, the combination of chemotherapy plus a biologic agent is the most suitable first-line treatment for patients with mCRC. The addition of the anti-EGFR mAb to the chemotherapy backbone is the most common treatment of RAS-wild-type mCRC. A number of different approaches involving biologic agents as single-agent¹² or in combination with chemotherapy regimens, and have made the choice of the 'best backbone' for first-line therapy', as well as the 'best biologic agent' to be added to the backbone, a key decision-making

the development of combination chemotherapy regimens including 5-FU led to the choice of... perspectives, evidence-based... therapy for

PATIENT:
age, fitness, personal motivation



PERSONALIZED TREATMENT?

The Oncologist®

Geriatric Oncology

Single-Agent Panitumumab in Frail Elderly Patients With Advanced *RAS* and *BRAF* Wild-Type Colorectal Cancer: Challenging Drug Label to Light Up New Hope

Age

Median (range)	81 (76–90)
75–79 years	15 (38)
80–84 years	21 (52)
85–89 years	3 (8)
90–94 years	1 (2)

Outcome	Overall population (<i>n</i> = 40)
Objective response rate, <i>n</i> (%)	13 (32.5%)
Disease control rate, <i>n</i> (%)	29 (72.5%)
Progression-free survival, median (95% CI)	6.4 months (4.9–8)
Overall survival, median (95% CI)	14.3 months (10.9–17.7)

OPEN ISSUES: SCORES AND CHEMO-INTENSITY

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Geriatric Factors Predict Chemotherapy Feasibility: Ancillary Results of FFCD 2001-02 Phase III Study in First-Line Chemotherapy for Metastatic Colorectal Cancer in Elderly Patients

Thomas Aparicio, Jean-Louis Jouve, Laurent Teillet, Dany Gargot, Fabien Subtil, Valérie Le Brun-Ly, Jacques Cretin, Christophe Locher, Olivier Bouché, Gilles Breysacher, Jacky Charneau, Jean-François Seitz, Mohamed Gasmi, Laetitia Stefani, Mohamed Ramdani, Thierry Lecomte, and Emmanuel Mitry

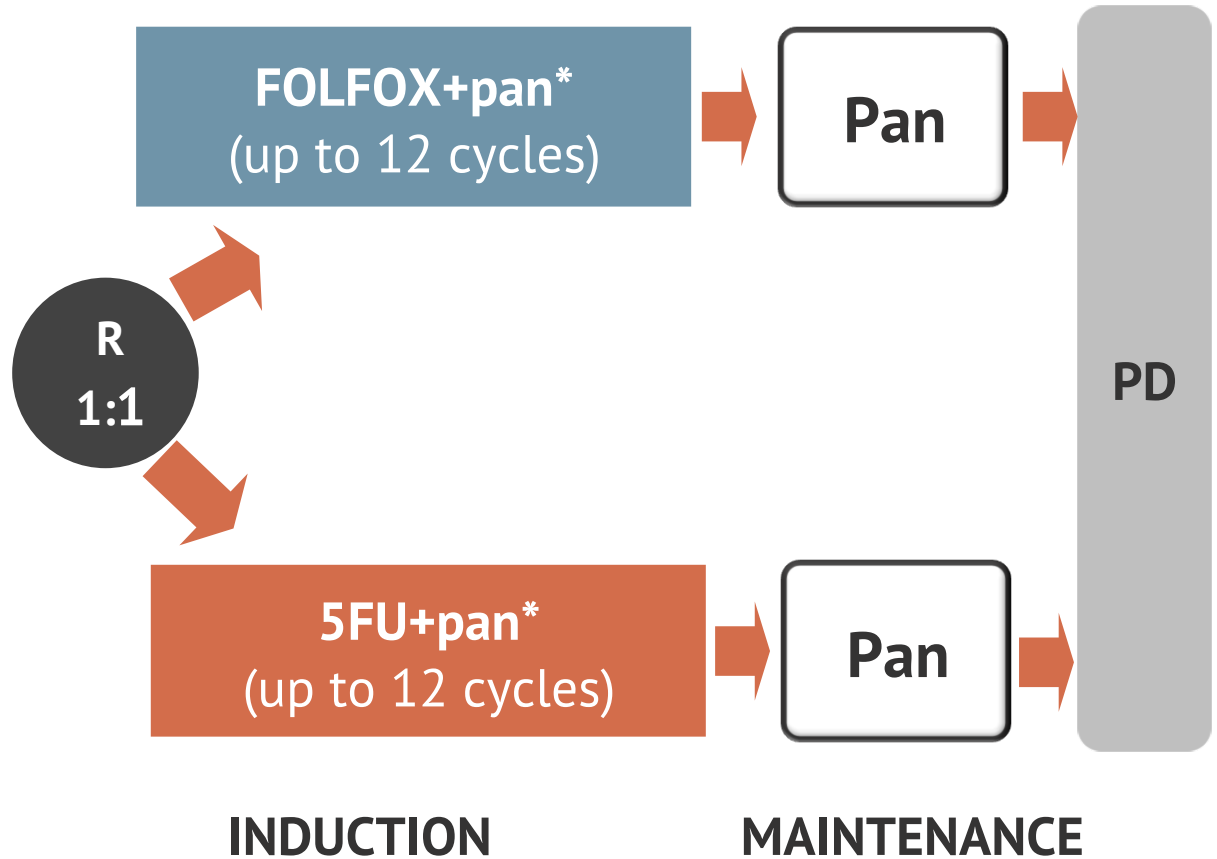
Randomized phase III trial in elderly patients comparing LV5FU2 with or without irinotecan for first-line treatment of metastatic colorectal cancer (FFCD 2001-02)[†]

T. Aparicio^{1*}, S. Lavau-Denes², J. M. Phelip³, E. Maillard⁴, J. L. Jouve⁵, D. Gargot⁶, M. Gasmi⁷, C. Locher⁸, X. Adhoute⁹, P. Michel¹⁰, F. Khemissa¹¹, T. Lecomte¹², J. Provençal¹³, G. Breysacher¹⁴, J. L. Legoux¹⁵, C. Lepère¹⁶, J. Charneau¹⁷, J. Cretin¹⁸, L. Chone¹⁹, A. Azzedine²⁰, O. Bouché²¹, I. Sobhani²², L. Bedenne^{4,5} & E. Mitry^{23,24} for FFCD investigators

STUDY DESIGN

>70 years age
unresectable
mCRC pts
stratified by:

- age ≤ 75 versus > 75
- ECOG PS 0-1 versus 2
- G8 Score ≤ 14 versus > 14



*repeated every 2 weeks **for up to 12 cycles (6 months)**
followed by **maintenance** with **pan** until PD

MAIN MESSAGES

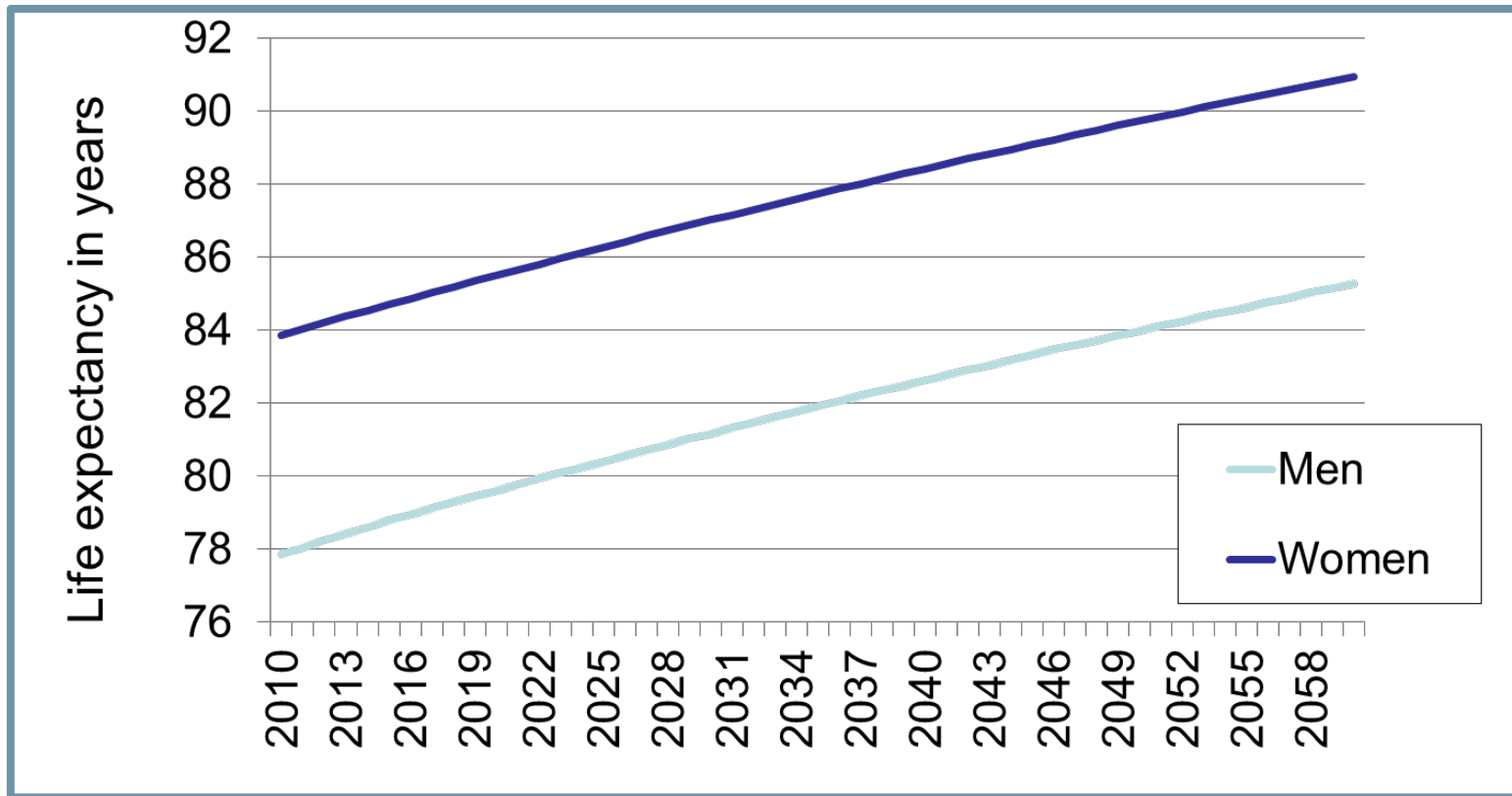
- Advanced age patients are not a “subgroup” of mCRC
- Current data support capecitabine plus bev as reasonable approach for the majority of elderly mCRC
- Data from small series support “personalized” approaches to selected pts
- Enrollment in clinical studies is strongly recommended
- Adapted chemo-intensification is under investigation
- Geriatric Scores (G8, CRASH, MMSE, IADL) should be implemented more and more in trials and in the clinic

UNFIT: A RELATIVE CONCEPT

by Prof. Hans Prenen
University Hospitals Leuven
Leuven, Belgium

LIFE EXPECTANCY

2010 - 2060



GERIATRIC SCREENING IN THE OLDER CANCER PATIENTS

Elderly = heterogeneous population

‘People are never more alike than they are **at birth**, no more different or unique than when they enter **the geriatric era**’



GERIATRIC POPULATION: QUESTIONS TO BE ASKED

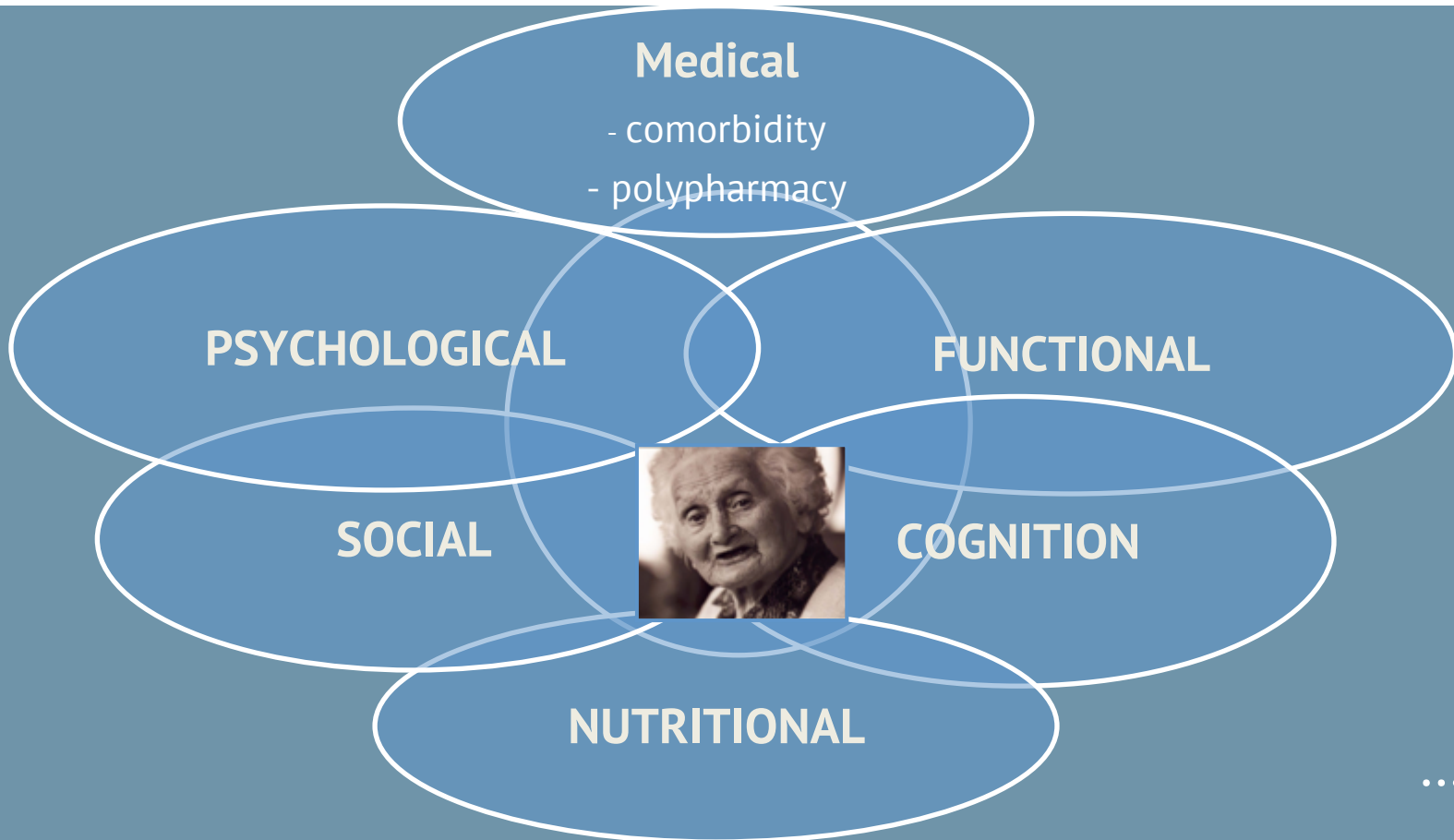


= a challenge!

- Does a geriatric assessment have therapeutic **consequences** with this patient?
- Is(n't) the patient **'to old'** for therapy?
- What is his/her **life expectancy**?
- Will he/she **tolerate the therapy**?
- Does the patient have **adequate social support** to sustain the treatment?
- ...

Independent
or not?????





Fit

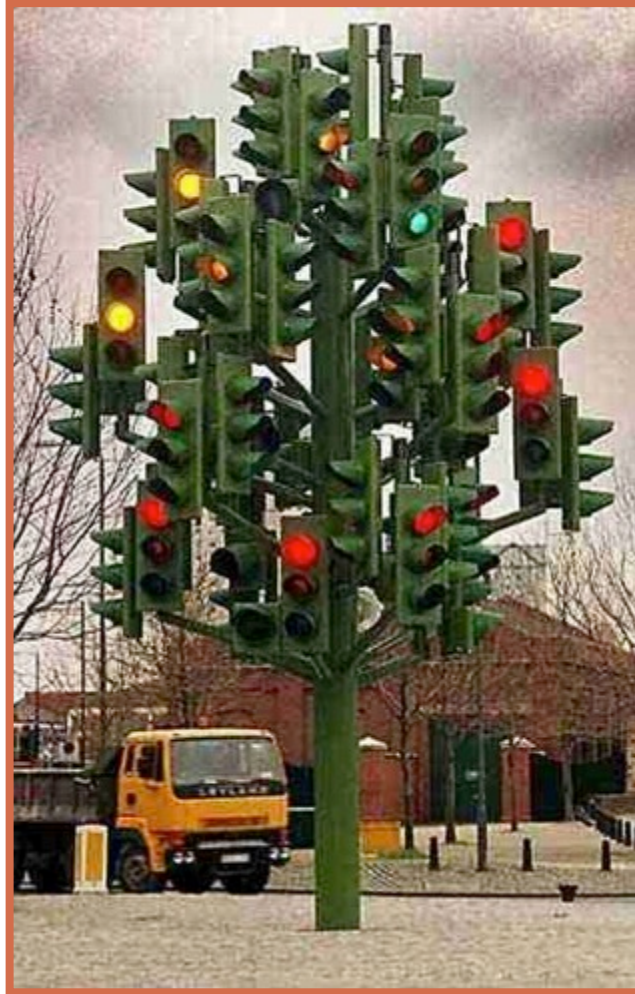


Unfit

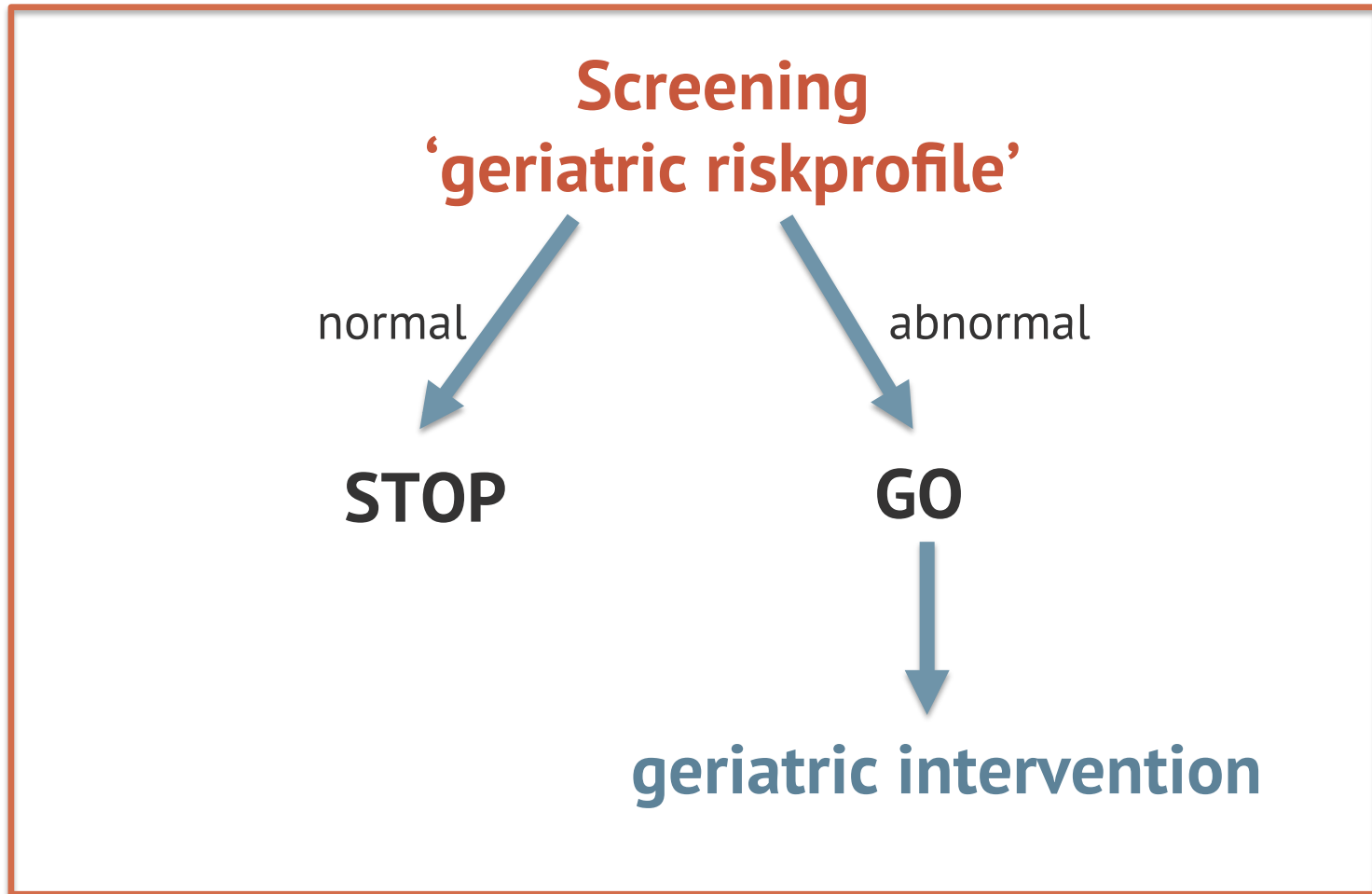
SCREENING FOR 'UNFIT'

ITEM	INSTRUMENT
Screening	Geriatric Risk Profile Instrument (GRP) G8 Groninger Frailty Index (GFI) Vulnerable Elders Survey-13 (VES-13) Senior Adult Oncology Program-2 (SAOP-2) Abbreviated CGA (aCGA) ...

AND WHAT NEXT...?



APPROACH IN THREE STEPS



GERIATRIC INTERVENTIONS

Contact other professional caregivers:

- General practitioner
- Social assistant
- Occupational therapist
- Physiotherapist
- Geronto-psychiatrist
- Dietician
- Psychologist
- ...



TAKE HOME MESSAGE

“It is better to do some kind of imperfect geriatric screening and assessment than doing no assessment at all...”





GI
connect

POWERED BY **COR2ED**