Ovarian Cancer in Advanced Age

A story of shared decisions and person-centered Care

Maria Cristina Petrella

Direttrice Oncologia Medica Ginecologica

Azienda Ospedaliera Universitaria Careggi

Disclosures

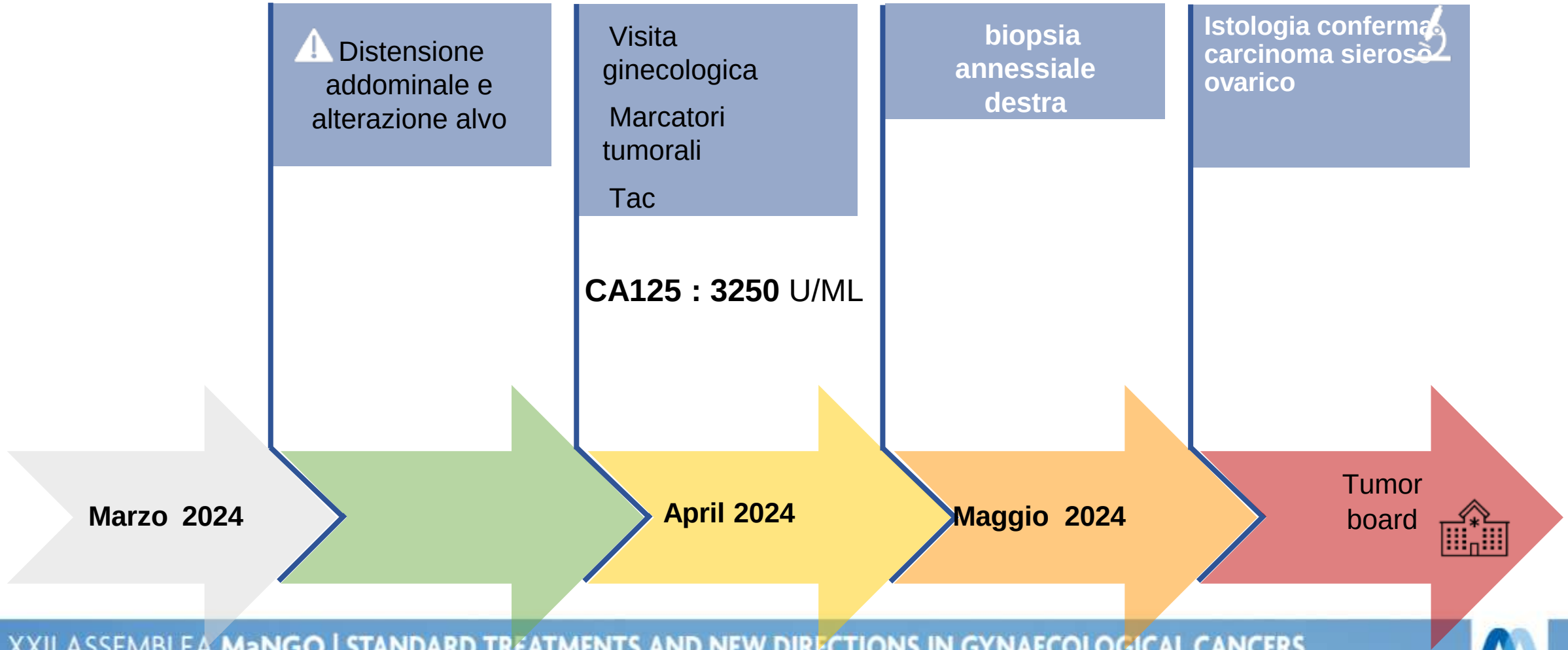
- *Speaking honoraria from: GSK, AstraZeneca, MSD, pharma&*
- *Advisory boards: GSK, AstraZeneca, MSD, eisai*

Storia di Carla

81 anni

- Anamnesi fisiologica : negativa
- H 158 cm L 75 kg, BMI 29,6
- Anamnesi ginecologica: G2PO Menopausa spontanea a 48 anni - No HRT
- Anamnesi familiare: nonna materna, zia e sorella con diagnosi di cancro al seno
- Anamnesi patologica remota: ipertensione arteriosa, ipercolesterolemia, appendicectomiacolecistectomia
- Stile di vita : Ex insegnante, Stile di vita attivo, Attività fisica, care giver presente
- Campionessa nazionale della sezione Anziani di Burraco

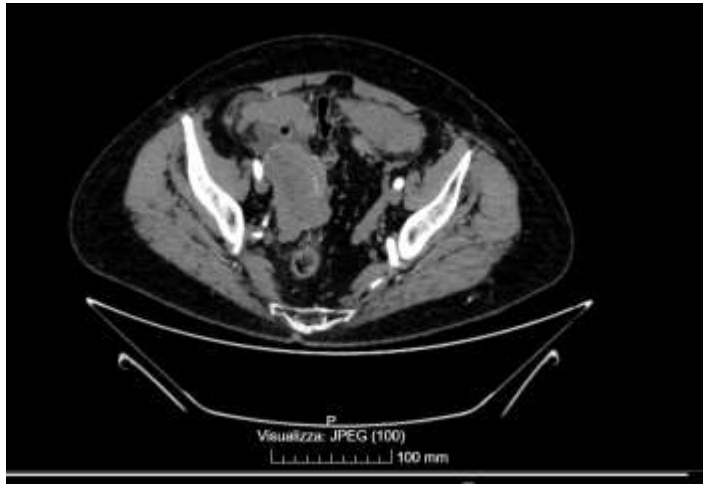
La storia di Carla



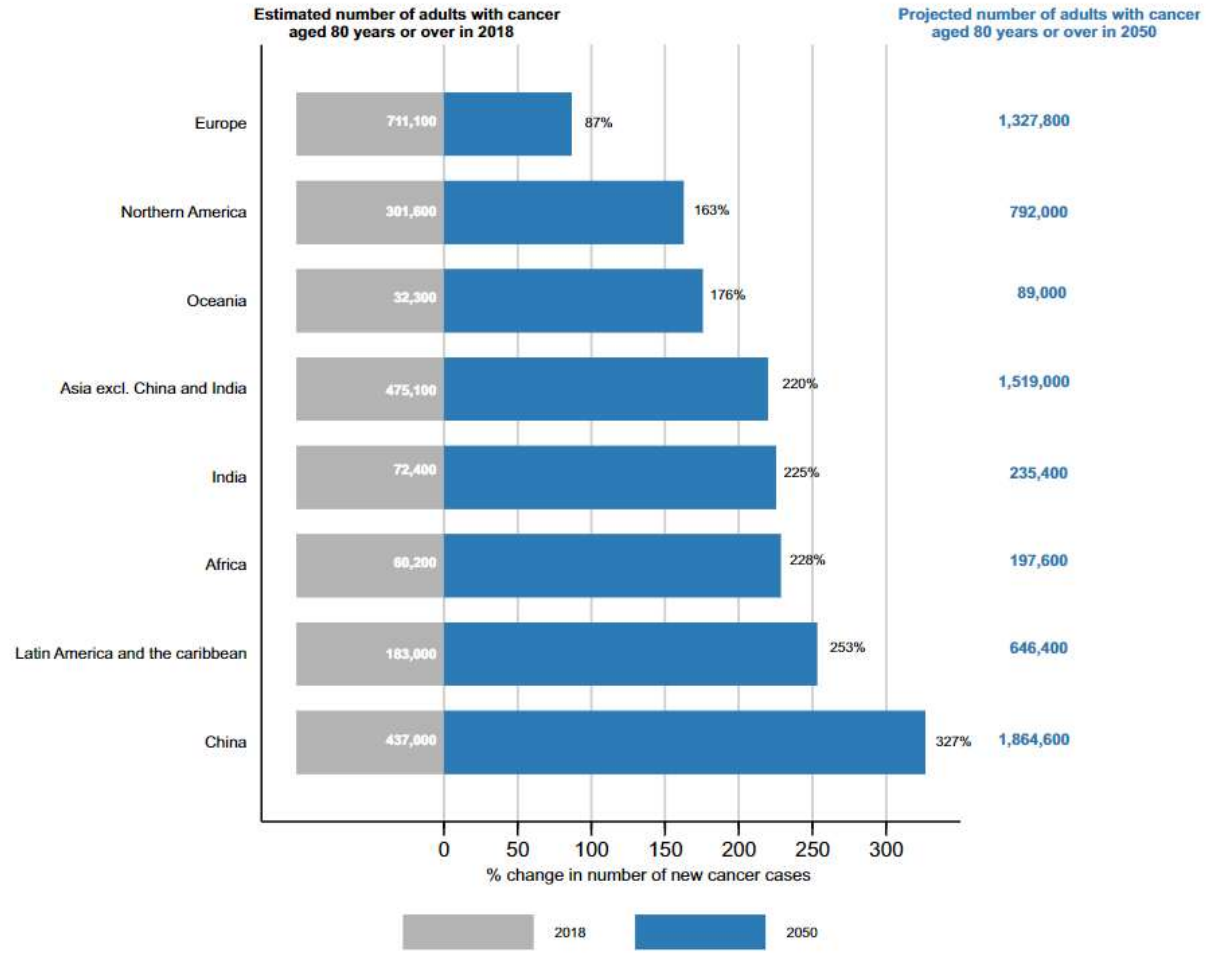
Esami di stadiazione

TC (18.04.2024)

- **Carcinomatosi peritoneale diffusa** con ispessimenti e nodularità multiple (maggiore pelvica: 70 mm).
- **Voluminosa massa pelvica destra** (94x70x60 mm), indissociabile dall'utero.
- **Versamento ascitico diffuso** (max 60 mm pelvico).
- **Nodulo polmonare** sospetto metastatico (8 mm, LID).
- **Versamento pleurico destro** (13 mm) con addensamento parenchimale associato.
- **Piccole nodularità epatiche e periepatica** sospette secondarie (8 mm).
- **Conclusione:**
  Quadro radiologico coerente con **malattia neoplastica avanzata (carcinomatosi peritoneale e metastasi polmonari/epatiche)**.



Estimated global cancer incidence in the Oldest Adults



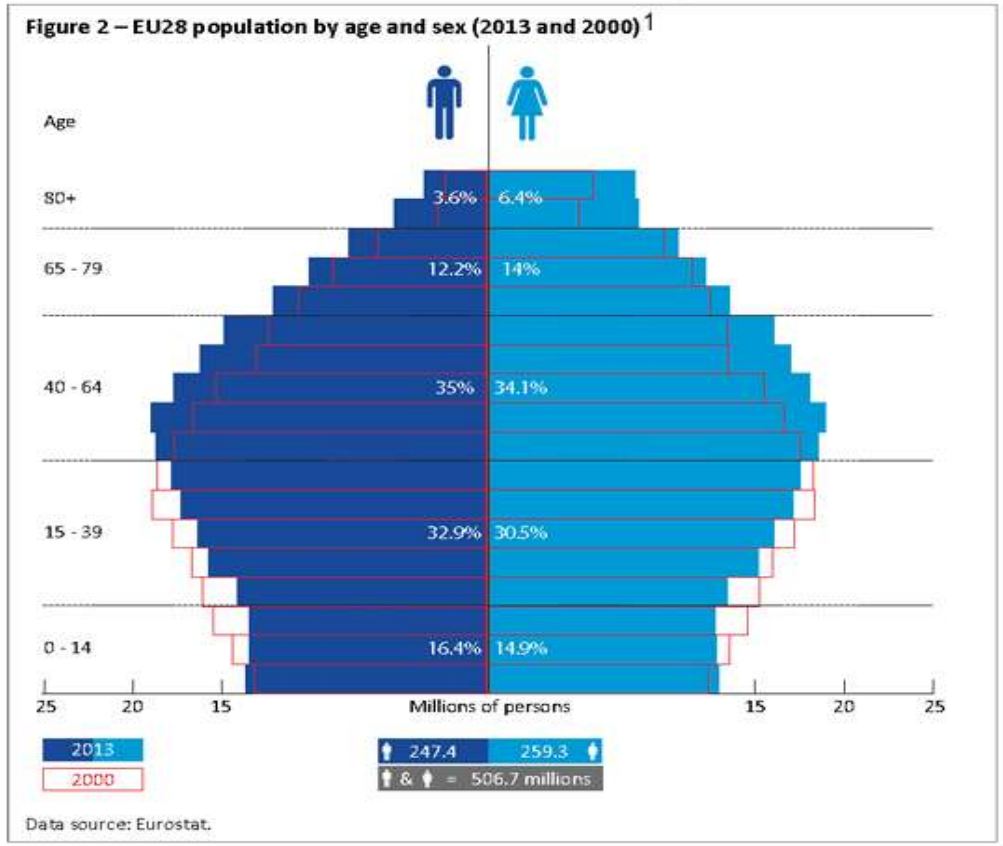
Pilleron S, et al. Int J Cancer 2020

«Silver tsunami» is coming

Kendal WS, et al. Cancer 2009
Bluethmann SM, et al. Cancer Epiemiol Biomarks Prev, 2016
Extermann M, et al. Lancet Oncol. 2021

GERIATRIC ONCOLOGY
Demographics of cancer and aging

Europe has a large older population…That will get even larger!



		Europe[2]
Population (in millions)	2007	591
	2050*	542
Population change 2007 to 2050, %		–8.3
Average age	2005	38.9
	2050*	47.3
Fertility rate	2006	1.50
Under 15 year olds, %	2007	16
	2050*	15
Over 65 year olds, %	2007	16
	2050*	28
Life expectancy	2006	76.0
	2050*	82.0

*Projection

Delivorias A, Sabbati G. EU Demographic Indicators: Situation, Trends And Potential Challenges, March 2015; https://epthinktank.eu/2015/03/20/eu-demographic-indicators-situation-trends-and-potential-challenges/; accessed Oct 2021. Copyright © European Union, 2014. All rights reserved; 2. Iris Hoßmann, Europe's Demographic Future Berlin Institut, 2008.

Geriatric Oncology

Approximately **70% of patients** with cancer are age 65 years and older.

J Clin Oncol. 2009 Jun 10; 27(17):2758-65

Less than **25% of patients** enrolled in National Cancer Institute Cooperative Group Clinical Trials are age 65 to 74 years, and less than 10% are 75 years or older.

J Clin Oncol. 2014 Aug 20; 32(24):2587-94.

vulnerable to **over-treatment** (ie, less fit patients given cancer treatment with low likelihood of benefit and high likelihood of complications/toxicity), **or under-treatment** (ie, fit older patients who are not given standard, evidence-based chemotherapy regimens)

Nat Rev Clin Oncol. 2012 Oct; 9(10):571-8.

traditional oncology performance measures, such as the Karnofsky or Eastern Cooperative Oncology Group performance status scores, **do not accurately predict** which older adults are at highest risk of adverse outcomes from chemotherapy

Cancer. 2005 Nov 1; 104(9):1998-2005

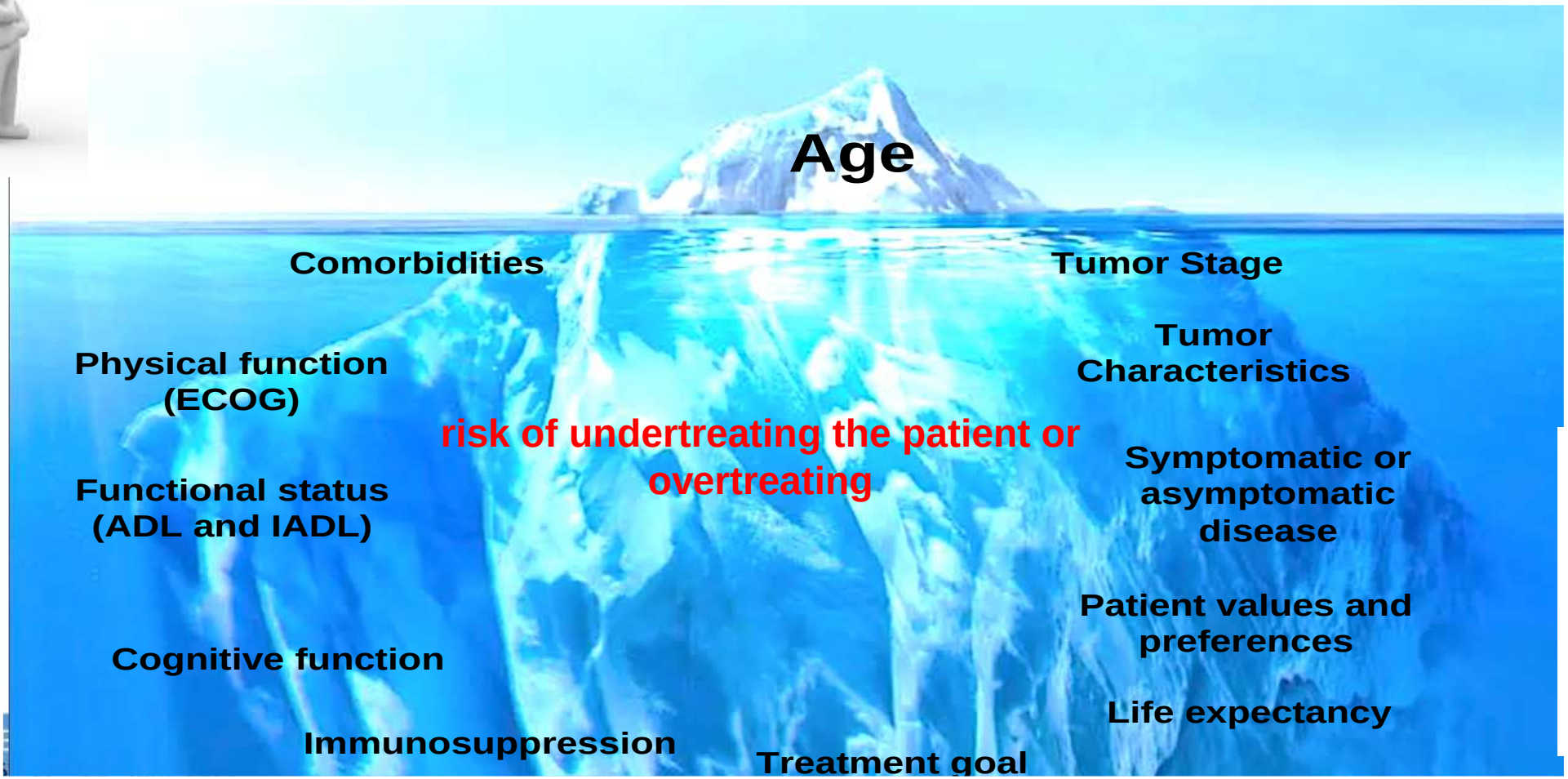
Older patients
with the same chronological age are different!

Genetics, lifestyle, socio-economic, mental and cultural issues all play a role!

Hurria A, et al. JCO 2011

A story of shared decisions and person-centered Care

Cancer in Elderly



ESMO

ESMO OPEN SCIENCE FOR OPTIMAL CANCER CARE

REVIEW

Adequate assessment yields appropriate care—the role of geriatric assessment and management in older adults with cancer: a position paper from the ESMO/SIOG Cancer in the Elderly Working Group

Consapevolezza: Conosce la diagnosi, la prognosi e parla in modo consapevole della propria malattia.
G8: 15 – In condizione di integrità
Indice di Barthel: 100
IADL: Pienamente conservate (8/8)
MMSE: 30/30 (funzione cognitiva nella norma)
GDS: 6/15
ECOG: 0 (ottima autonomia)
MNA SF: 14 – Stato nutrizionale nella norma (altezza 158 cm, peso 74 kg, BMI 29.6 – lieve sovrappeso, ben compensato)
Fragilità sec. Fried: 0 –
Non vulnerabile (velocità del cammino adeguata, forza muscolare nella norma – 19.4 Kg)
CIRS: Severità 2.08 – Comorbilità 5/14 (ben compensate)

Table 1. Geriatric assessment domains and tools

Geriatric assessment domain	Tools[a]	Interventions for positive finding
Functional status	• Self-reported: ◦ Activities of daily living ◦ Instrumental activities of daily living ◦ Falls • Objective tests: ◦ Timed up and go test ◦ Gait speed ◦ Short physical performance battery	1. Mobility and health aids 2. Home safety equipment 3. Promote physical activity 4. Physical therapy and rehabilitation
Comorbidity	• Charlson Comorbidity Index • Cumulative Index Rating Scale-Geriatric • Adult Comorbidity Evaluation-27	1. Comorbidity management 2. Referral to a geriatrician or other specialists 3. Clarify goals of care
Social functioning and support	• Medical Outcomes Study survey • RAND-36 Healthcare Survey	1. Consult social work 2. Consult financial services
Cognition	• Blessed Orientation Memory Concentration test • Mini Cog • Mini Mental State Examination • Montreal Cognitive Assessment	1. Counseling 2. Assess inappropriate medications 3. Evaluate decisional capacity 4. Referral to geriatric neuropsychologist
Psychological status	• Distress Thermometer • Geriatric Depression Scale (several versions available) • Mental Health Inventory • Patient Health Questionnaire (several versions available)	1. Cognitive behavioral therapy 2. Non-pharmacological approaches (meditation) 3. Anti-depressants 4. Referral to a geriatric psychiatrist 5. Communicate with primary care team
Nutrition	• Weight loss • Body mass index • Mini Nutritional Assessment • Malnutrition Universal Screening Tool	1. Address factors contributing to malnutrition 2. Address chemotherapy-induced adverse effects like nausea/vomiting 3. Oral care 4. Supplemental nutrition 5. Refer to dietitian
Polypharmacy	• Beers Criteria • Medication Appropriateness Index • STOPP/START criteria	1. Medication reconciliation 2. Evaluate adherence 3. Evaluate drug interactions 4. Deprescribing 5. Home health for medication management

START, Screening Tool to Alert to Right Treatment; STOPP, Screening Tool of Older Persons' Prescriptions.
[a]At a minimum, consider one tool from the domains of functional status (instrumental activities of daily living), cognition (Mini Cog or Blessed Orientation Memory Concentration), and psychological status (PHQ-2); assess weight loss, comorbidity, and medications from the medical records; and inquire about source of social support from the patient.

In data odierna viene effettuata valutazione fisioterapica e saranno date indicazioni sull'attività fisica da svolgere al domicilio, rivalutazione prevista in corso di decisione terapeutica

Discussione multidisciplinare → TRATTAMENTO NEOADIUVANTE

- **BRCA WT , HRDd**
- Maggio 2024- agosto 2024 cicli di chemioterapia IV con carboplatino AUC5 e paclitaxel 175 mg/m2 (riduzione del 20% di paclitaxel)
- Il paziente ha iniziato l'agopuntura settimanale per controllare nausea, astenia e neuropatia accompagnata dal caregiver
- Ha avviato percorso pre-hab
- Ha continuato con i tornei di burraco che sicuramente hanno aiutato con la **CHEMO-BRAIN**
- Tossicità del trattamento: anemia G1, astenia G1, mucosite G1, neuropatia G1

Title: The Use of Virtual Reality in Oncology: Effects on Anxiety, Pain, and Discomfort During Chemotherapy in Patients with Gynecologic Cancer

GO CARE
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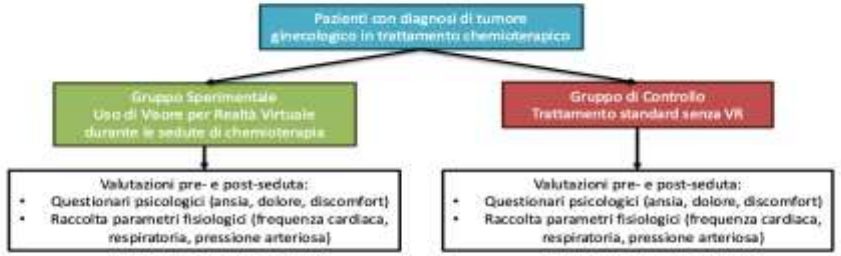
Azienda Ospedaliero Universitaria Careggi

L'utilizzo della realtà virtuale in oncologia

STUDIO CLINICO OSSERVAZIONALE PROSPETTICO

OBIETTIVO: valutare se l'uso della Realtà Virtuale (VR) durante le sedute di chemioterapia possa aiutare a ridurre ansia, dolore e discomfort nei pazienti con diagnosi di tumore ginecologico.



Misure PRE-trattamento	Misure POST-trattamento
Questionari psicologici ➢ Hospital Anxiety and Depression Scale (HADS) ➢ Termometro del Distress ➢ Generalized Anxiety Disorders-7 (GAD-7) ➢ Numeric Pain Rating Scale (NPRS)	**Questionari psicologici** ➢ Termometro del Distress ➢ Generalized Anxiety Disorders-7 (GAD-7)
Parametri fisiologici ➢ Frequenza cardiaca (HR) ➢ Frequenza respiratoria (BR) ➢ Pressione arteriosa (BP)	**Parametri fisiologici** ➢ Frequenza cardiaca (HR) ➢ Frequenza respiratoria (BR) ➢ Pressione arteriosa (BP)

L'utilizzo della realtà virtuale in oncologia

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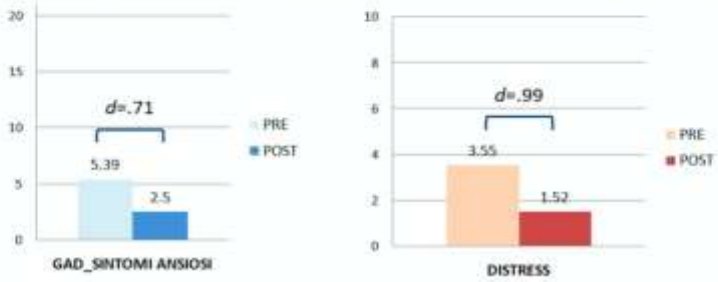
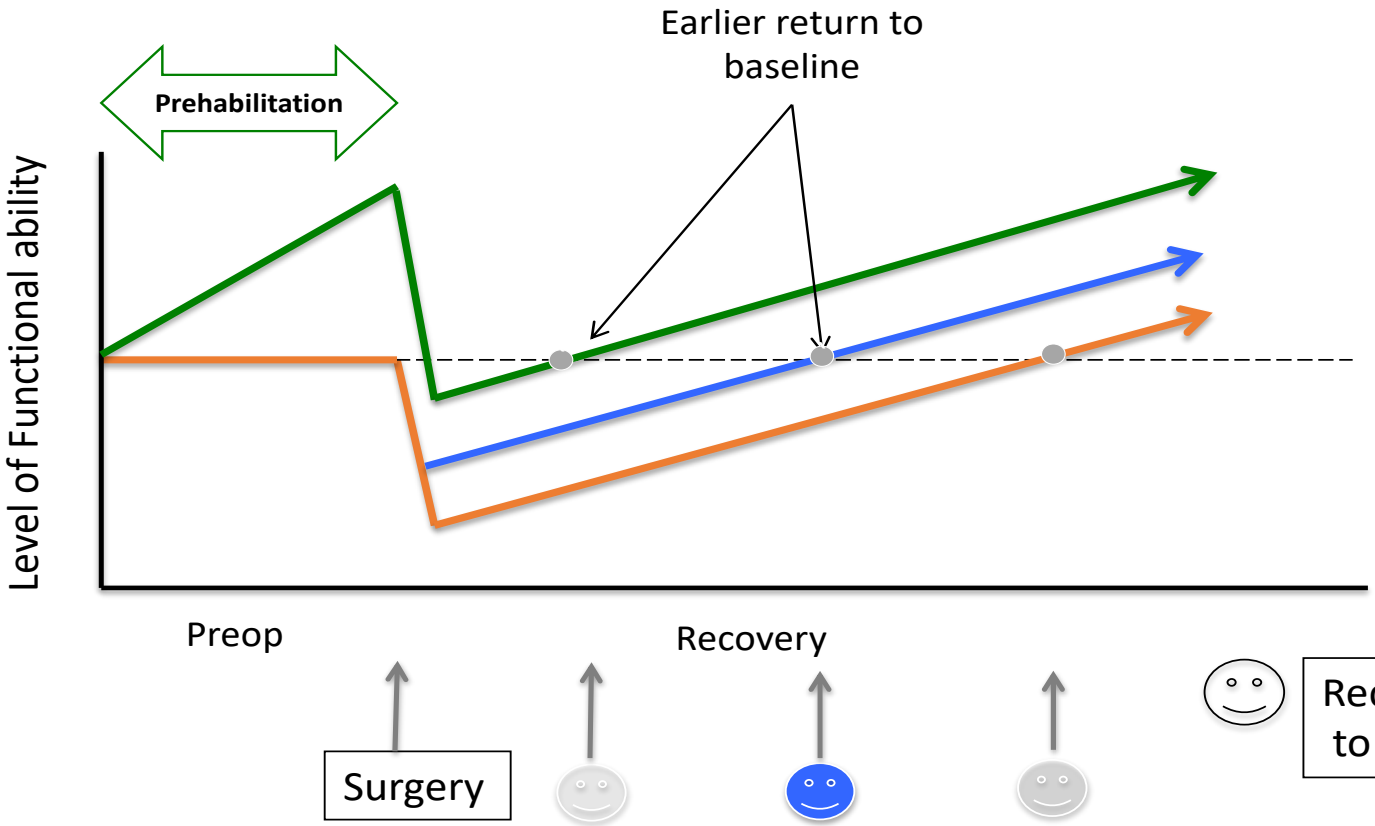
DIFFERENZE PRE-POST APPLICAZIONE

FREQUENZA CARDIACA PRE	FREQUENZA CARDIACA POST
M(DS)=77.74(10.93); range 52-95	M(DS)=75.47(11.15); range 50-91



Surgical Prehabilitation-Recovery begins before surgery
Transform “waiting” time in “preparation” time !



Prehab + ERAS

Enhanced Recovery After Surgery (ERAS)

Traditional care

Recovery = time to recovery to baseline

Carli et al. Anesthesiology Clin 33 (2015) 17–33

Multimodal Preoperative Optimization: Prehabilitation

Frequency
Intensity
Type
Time
Progression

Exercises/Personalized
3 times/week
- AEROBIC Training *
- RESISTANCE Train
- BALANCE Train
- IMT (High pulm. risk)

Nutrition counselling based on 3-day food record
- BALANCED Meal
- PROTEIN**
- ✓Energy requirements (25-30 Kcal/day) **
- WHEY PROTEIN (20g >)
- Vit D
- Immunonutrition

Anxiety & depression, Cognitive optimization
- Reinforce program
- Breathing exercise
- Audio-track
- Cognitive behavioral therapy
- Mindfulness
- Cognitive Prehabilitation

Medical Optimization
- Anemia
- Diabetes
- Heart Failure
- COPD
- Smoking/Alcohol cessation
- Geriatric Syndroms

*High Intensity Interval Training (HIIT)
Moderate Continuous Training (MCT)

** **even HIGHER!**

LA STORIA DI CARLA

LUGLIO 2024: TC torace addome con mdc (dopo III cicli di terapia)

•Area Ground Glass (GGO) invariata all'apice polmonare sinistro, da monitorare nel tempo. Presenza di alcuni micronoduli polmonari bilaterali, il più grande di 3 mm alla lingula, stabili. Assenza di nuove lesioni sospette nei polmoni. Linfonodo pericardiofrenico destro millimetrico, stabile rispetto a precedente valutazione.
•Non evidenti linfonodi patologici nel mediastino e agli ili polmonari. Non versamento pleurico.
Addome e pelvi: Assenza di lesioni sospette negli organi solidi (fegato, milza, pancreas, surreni, reni). Esiti di colecistectomia con modesta dilatazione delle vie biliari (coledoco 13 mm)
•Diverticoli del sigma. Utero disomogeneo.
•Notevole riduzione della tumefazione annessiale destra: ora di 40 mm rispetto ai precedenti 77 mm.
•Assenza di linfoadenomegalie retroperitoneali, lombo-aortiche o pelviche. Assenza di ascite.
•Miglioramento del quadro di carcinosi peritoneale con residuo di "omental cake" ridotto a 11 mm e lieve ispessimento del peritoneo pelvico.

•KELIM FAVOREVOLE

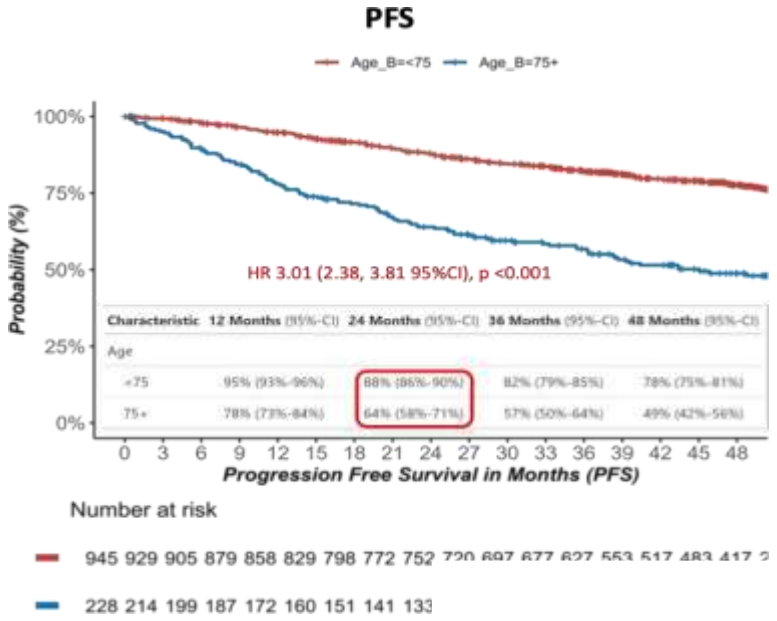
•PS 1

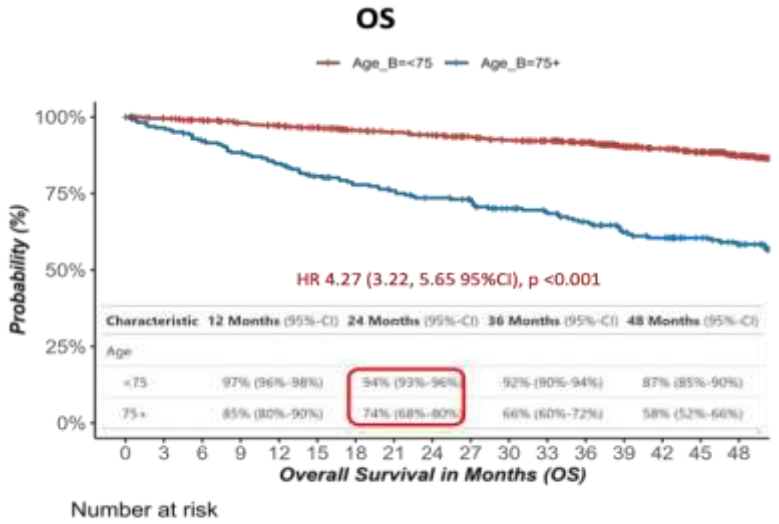
•VALUTAZIONE ONCOGERIATRICA : quadro stabile

Treatment and Outcome of Elderly Patients with Early Ovarian Cancer in Germany – QS Ovar of the AGO Study Group

Progression Free Survival (PFS) and Overall Survival (OS)

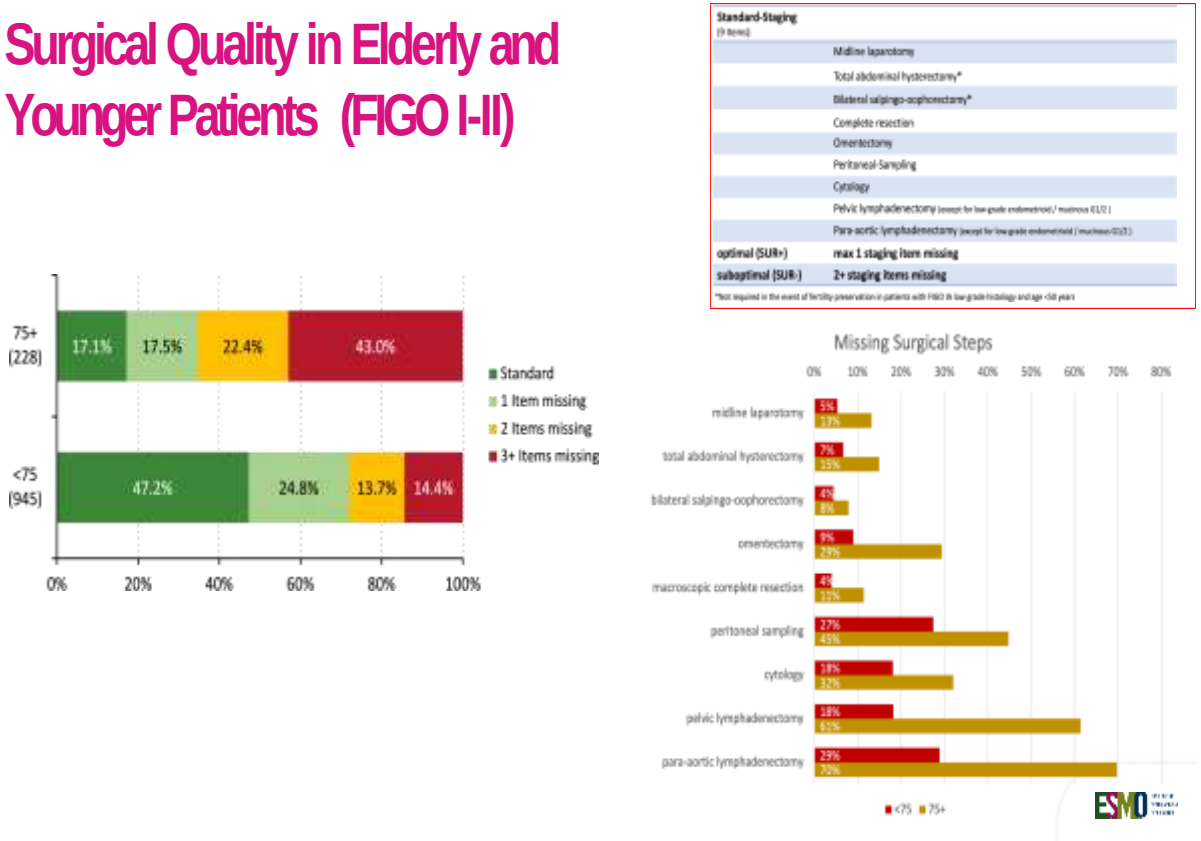
<75 vs. 75+ Yrs





IDS in paziente anziana affetta da carcinoma ovarico avanzato

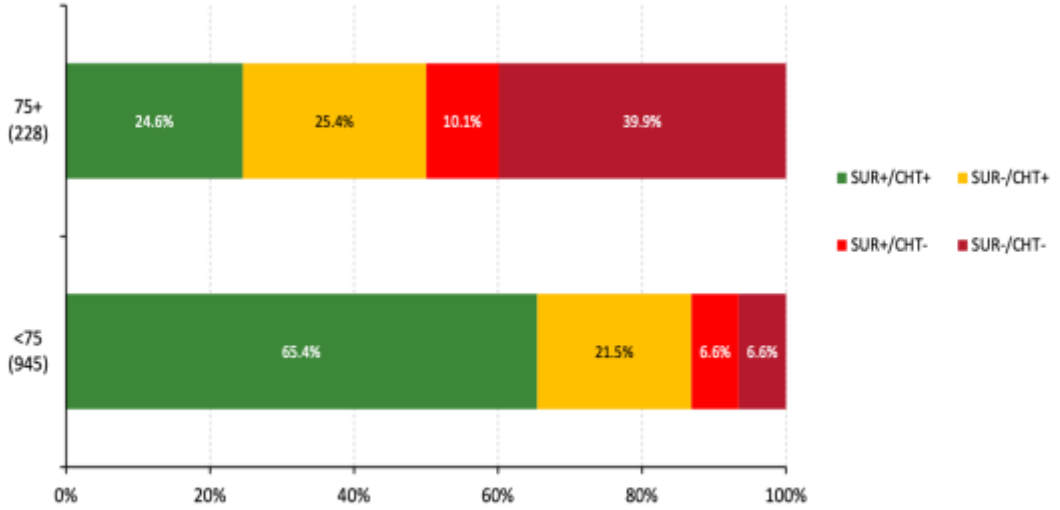
Data 25/09/2024. ISTERECTOMIA TOTALE EXTRAFASCIALE - ANNESSIECTOMIA BILATERALE - DEPERITONEIZZAZIONE DELLA PLICA PREVESCICALE - DEL PERITONEO DEL DOUGLAS E DELLE DOCCE PARACOLICHE- - OMENTECTOMIA INFRAGASTROCOLICA - CITOLOGIA PERITONEALE **(CHIRURGIA MINI-INVASIVA ROBOTICAMENTE ASSISTITA)** ADENOCARCINOMA SIEROSO DI ALTO GRADO EXTRAUTERINO POST NACT
CRS 2



Treatment and Outcome of Elderly Patients with Early Ovarian Cancer in Germany – QS Ovar of the AGO Study Group

Combined Quality of Treatment in Elderly and Younger Patients

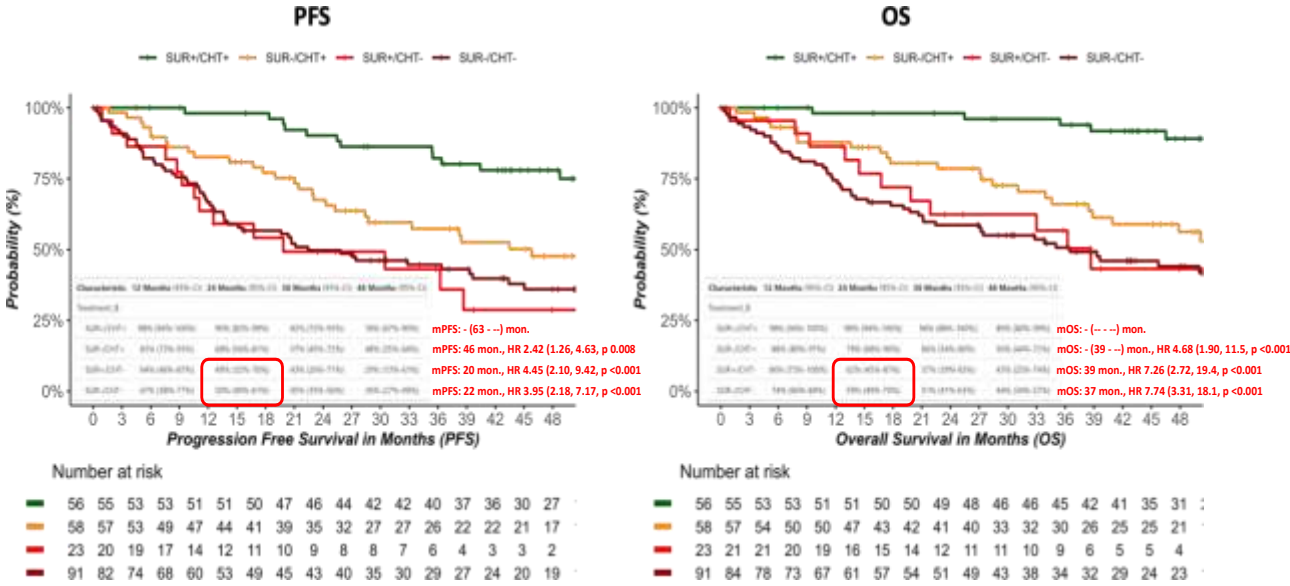
CHT+: chemotherapy "standard soft", SUR+= surgery max 1 Item missing



Felix Hilpert

Elderly Treatment Combined: Outcome

CHT+: chemotherapy "standard soft", SUR+= surgery max 1 Item missing



TERAPIA DI MANTENIMENTO→ discussione e condivisione con la paziente PAZIENTE Carboplatino in monoterapia e bevacizumab poi mantenimento con bavacizumab e olaparib PAOLA 1

Punti di discussione

HRDd ,kelim favorable ,CRS2, STADIO IIIB R0

Buona risposta al platino

Monoterapia o terapia combinata

Tossicità al trattamento

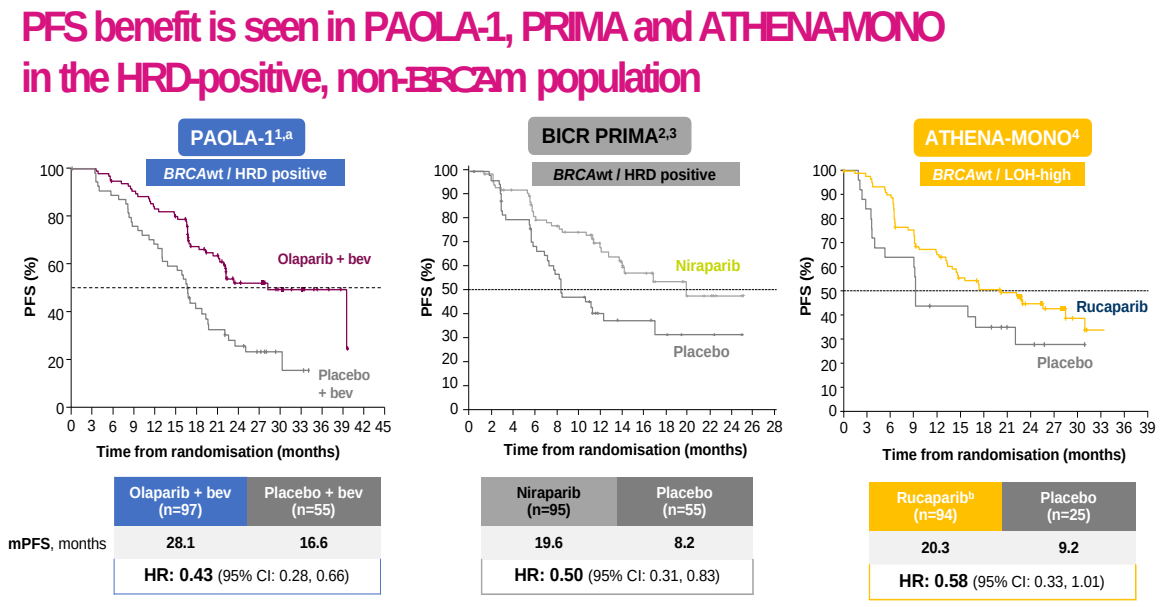
Compliance al trattamento

Aspettativa di vita

OS o PFS

Possibilità di descalation al trattamento

Costi



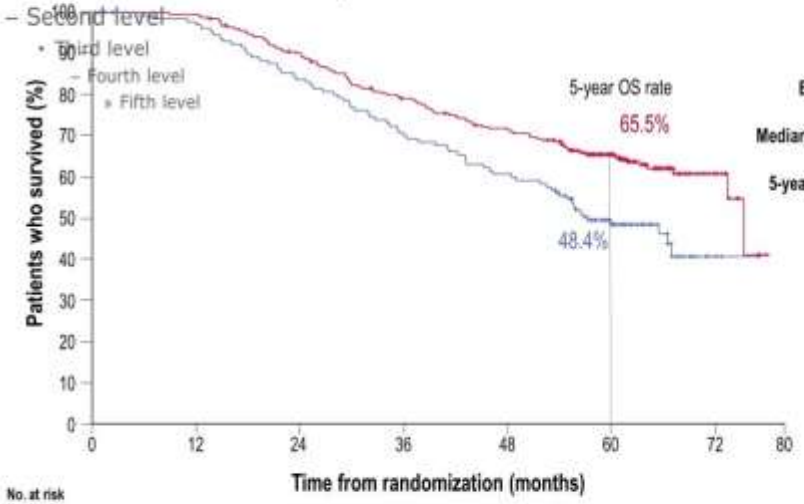
oquard et al, Ann Oncol 2023, 2,3 T Herzog, et al IJGC 2023 4B Monk ASCO 2022

se.

Is Overall survival plays a role?

OS was prolonged in the HRD-positive subgroup

- Click to edit Master text styles
  - Second level
    - Third level
      - Fourth level
        - Fifth level



	Olaparib + bevacizumab (N=255)	Placebo + bevacizumab (N=132)
Events, n (%)	93 (36.5)	69 (52.3)
Median OS, months	75.2 (unstable)*	57.3
5-year OS rate, %	65.5	48.4

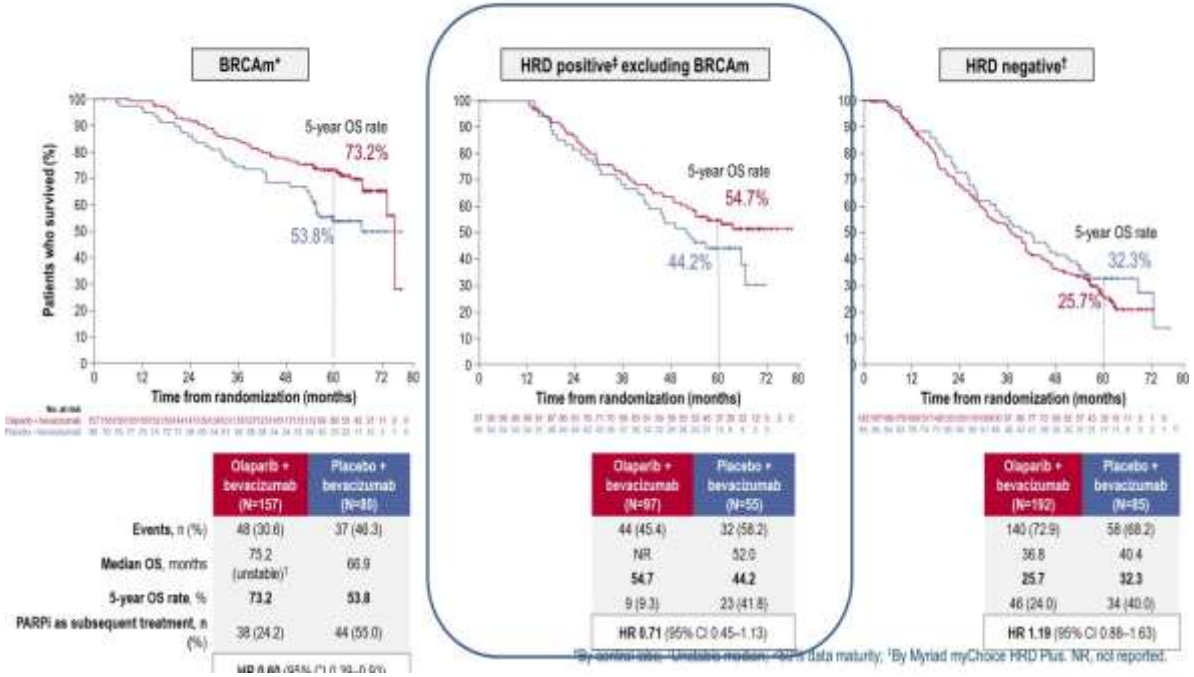
HR 0.62 (95% CI 0.45–0.85)

38% reduction in risk of death for olaparib + bevacizumab vs bevacizumab alone

Patients receiving a PARP inhibitor during any subsequent treatment
Olaparib + bevacizumab: **17.3%** (44/255)
Placebo + bevacizumab: **50.8%** (67/132)

*Median unstable; <50% data maturity.
HRD positive defined as a tBRCAm and/or genomic instability score of ≥42 on the Myriad myChoice HRD Plus assay.

PAOLA-1 OS subgroup analysis by BRCAm and HRD status



	Olaparib + bevacizumab (N=157)	Placebo + bevacizumab (N=80)	Olaparib + bevacizumab (N=97)	Placebo + bevacizumab (N=55)	Olaparib + bevacizumab (N=192)	Placebo + bevacizumab (N=85)
Events, n (%)	48 (30.6)	37 (46.3)	44 (45.4)	32 (58.2)	140 (72.9)	58 (68.2)
Median OS, months	75.2 (unstable)†	66.9	NR	52.0	36.8	40.4
5-year OS rate, %	73.2	53.8	54.7	44.2	25.7	32.3
PARPi as subsequent treatment, n (%)	38 (24.2)	44 (55.0)	9 (9.3)	23 (41.8)	46 (24.0)	34 (40.0)
			HR 0.71 (95% CI 0.45–1.13)		HR 1.19 (95% CI 0.88–1.63)	

*By central site; †Unstable median, <50% data maturity; ‡By Myriad myChoice HRD Plus; NR, not reported.

European Journal of Cancer 181 (2023) 42–52

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Original Research

Efficacy and safety of maintenance olaparib and bevacizumab in ovarian cancer patients aged ≥65 years from the PAOLA-1/ENGOT-ov25 trial

Demographics of patients included in the olaparib arm according to age.

Clinical and pathological features at inclusion		≥65 years (n = 205)	<65 years (n = 332)	P value
Median age at baseline, years (minimum–maximum)		70 (65–87)	56 (32–64)	
ECOG performance status	0	125 (61.0)	253 (76.2)	0.0005
	1	76 (37.1)	77 (23.2)	
	Missing	4 (2.0)	2 (0.6)	
FIGO stage	III	149 (72.7)	229 (69.0)	0.38
	IV	56 (27.3)	103 (31.0)	
BRCA deleterious mutation	All	35 (17.1)	122 (36.7)	<0.0001
	BRCA1	15 (7.3)	96 (28.9)	
	BRCA2	20 (9.8)	25 (7.5)	
	BRCA1 and *BRCA2*	0 (0.0)	1 (0.3)	
HRD status	Positive	70 (34.1)	185 (55.7)	<0.0001
	Negative	101 (49.3)	91 (27.4)	
	Unknown	34 (16.6)	56 (16.9)	
Upfront surgery		86 (42.0)	185 (55.7)	0.0025
	Residual macroscopic disease	39 (45.3)	72 (38.9)	0.35
	No residual macroscopic disease	47 (54.7)	113 (61.1)	
First-line treatment outcomes	NED with complete cytoreduction at primary DS	46 (22.4)	112 (33.7)	0.063
	NED/CR with complete cytoreduction at interval DS	64 (31.2)	94 (28.3)	
	NED/CR with incomplete resection or no DS	29 (14.1)	50 (15.1)	
	PR	62 (30.2)	72 (21.7)	
	Missing	4 (2.0)	4 (1.2)	

Data are n (% of cases with data available) unless otherwise specified.
Abbreviations: CR, complete response; DS, debulking surgery; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; HRD, homologous recombination deficiency; NED, no evidence of disease; PR, partial response.

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Original Research

Efficacy and safety of maintenance olaparib and bevacizumab in ovarian cancer patients aged ≥65 years from the PAOLA-1/ENGOT-ov25 trial

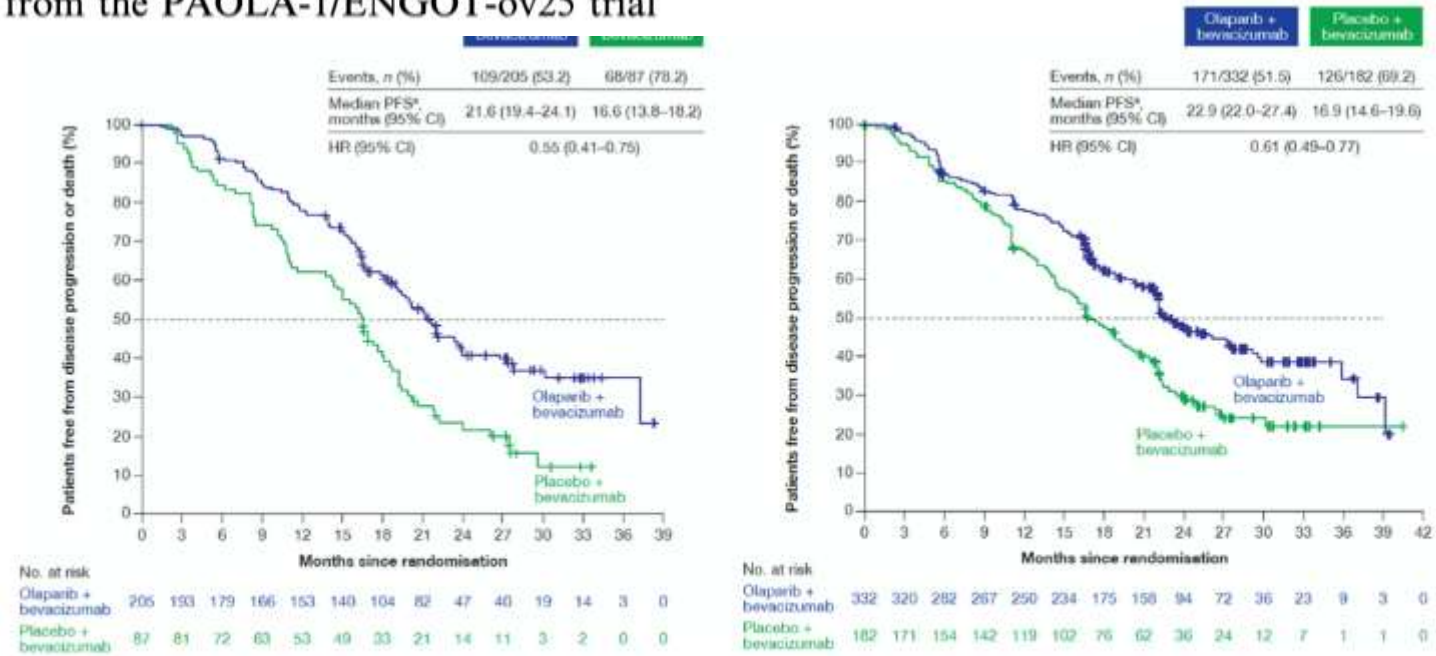
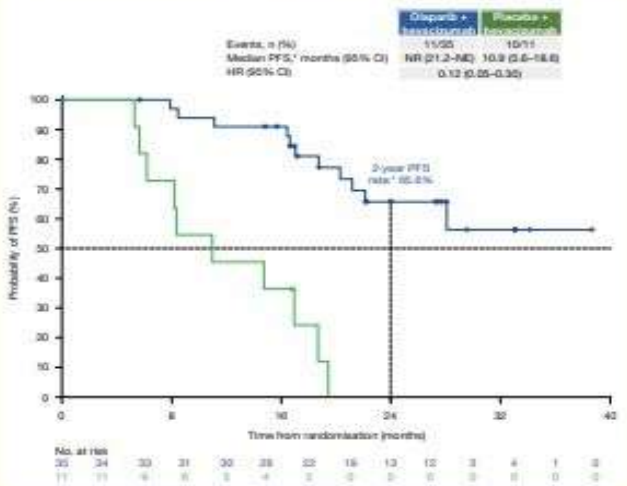


Fig. 1. Kaplan–Meier curves for PFS in the intention-to-treat population. (A) Older patients (aged ≥65 years). (B) Younger patients (aged <65 years). *Abbreviations*: CI, confidence interval; HR, hazard ratio; PFS, progression-free survival. [a]Estimated using the Kaplan–Meier method; HRs estimated using a multivariate Cox model.

Elderly more than 70 years old

Figure 3. PFS among older patients (≥70 years old) with HRD-positive tumours in PAOLA-1



*Estimated using the Kaplan–Meier method. HRD was defined as a tBRCAm or a genomic instability score ≥42. NE, not estimable; NR, not reached.

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Original Research

Efficacy and safety of maintenance olaparib and bevacizumab in ovarian cancer patients aged ≥65 years from the PAOLA-1/ENGOT-ov25 trial

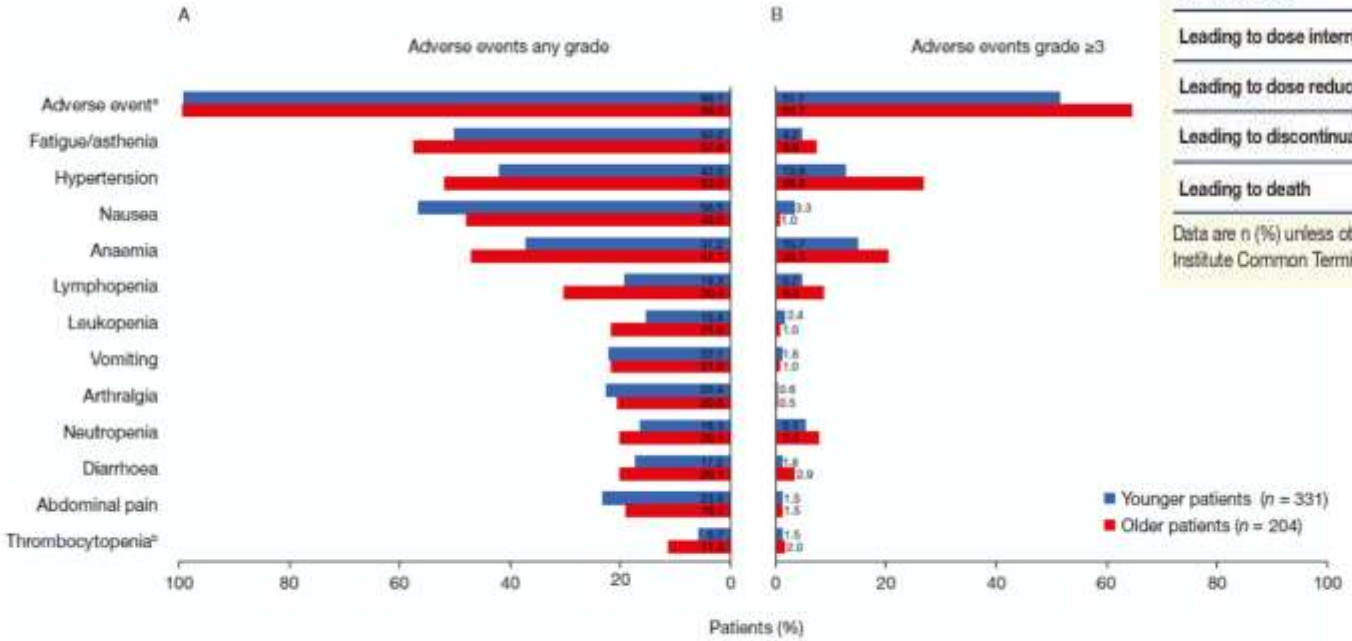


Fig. 4. Most frequent AEs in the olaparib arm by age. (A) All-grade AEs. (B) Grade ≥3 AEs. *Abbreviation*: AE, adverse event. [a]Overall incidence of AEs of any grade (left-hand panel) and grade ≥3 (right-hand panel). [b]Occurred in <20% of patients in either age group, but included to provide more complete information on the haematological safety profile.

Table 3. Summary of TRAEs by GVS and treatment arm in older patients (≥70 years old)

TRAEs	GVS 0		GVS ≥1	
	Olaparib (n=34)	Placebo (n=12)	Olaparib (n=48)	Placebo (n=18)
Grade ≥3	13 (38.2)	1 (8.3)	22 (45.8)	4 (22.2)
Serious TRAEs	6 (17.6)	0	12 (25.0)	3 (16.7)
Leading to dose interruption	14 (41.2)	4 (33.3)	28 (58.3)	3 (16.7)
Leading to dose reduction	10 (29.4)	1 (8.3)	25 (52.1)	4 (22.2)
Leading to discontinuation	10 (29.4)	1 (8.3)	11 (22.9)	1 (5.6)
Leading to death	0	0	0	0

Data are n (%) unless otherwise stated. Relationship to the indicated agent was assessed by the investigator. AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 4.03. TRAEs, therapy-related adverse events.

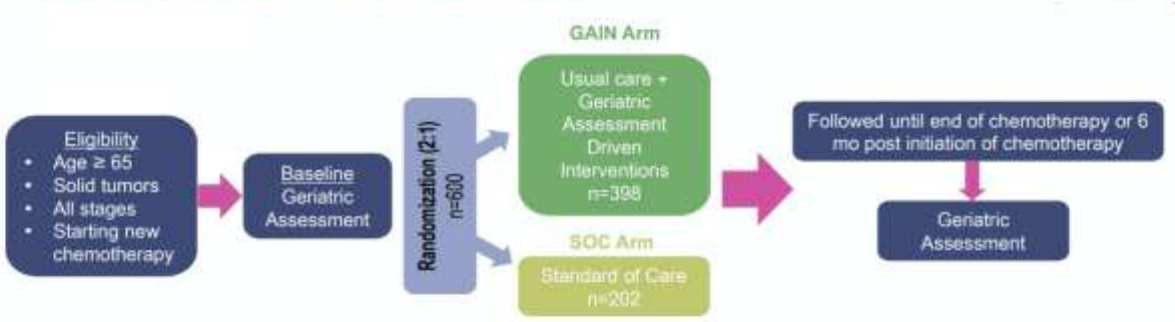
Impact of CGA on chemotoxicity (the GAIN trial)

Research

JAMA Oncology | Original Investigation

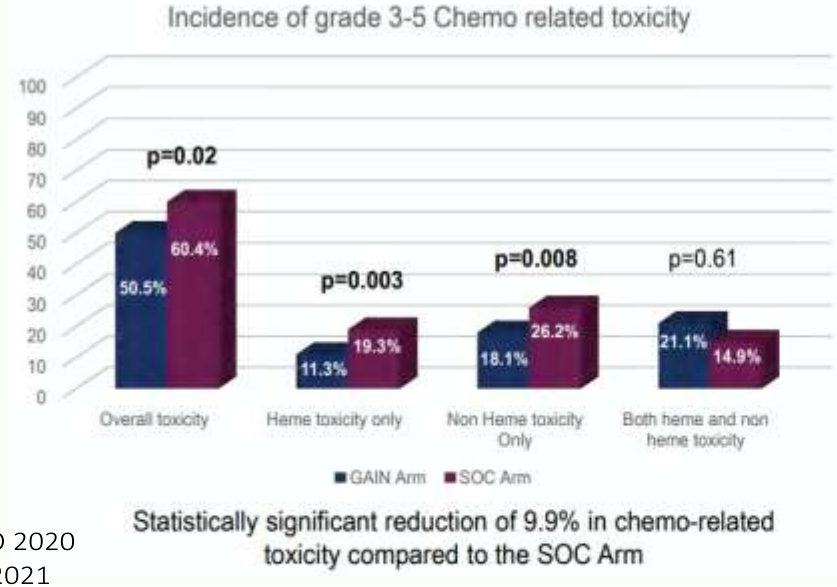
Geriatric Assessment–Driven Intervention (GAIN) on Chemotherapy-Related Toxic Effects in Older Adults With Cancer
A Randomized Clinical Trial

Daneng Li, MD; Can-Lan Sun, PhD; Heeyoung Kim, MPH; Enrique Soto-Perez-de-Celis, MD; Vincent Chung, MD; Marianna Koczywas, MD; Marwan Fakih, MD; Joseph Chao, MD; Leana Cabrera Chien, MSN; Kemeberly Charles, BS; Simone Fernandes Dos Santos Hughes, MD; Vani Katheria, MS; Monica Trent, BS; Elsa Roberts, BS; Reena Jayani, MD; Jeanine Moreno, MSN; Cynthia Kelly, MSN; Mina S. Sedrak, MD, MS; William Dale, MD, PhD



Primary endpoints:
- Incidence of grade 3-5 chemotoxicity

Secondary endpoints:
- Advance directive completion
- Unplanned hospitalizations
- ER visits
- Average length of stay



Statistically significant reduction of 9.9% in chemo-related toxicity compared to the SOC Arm

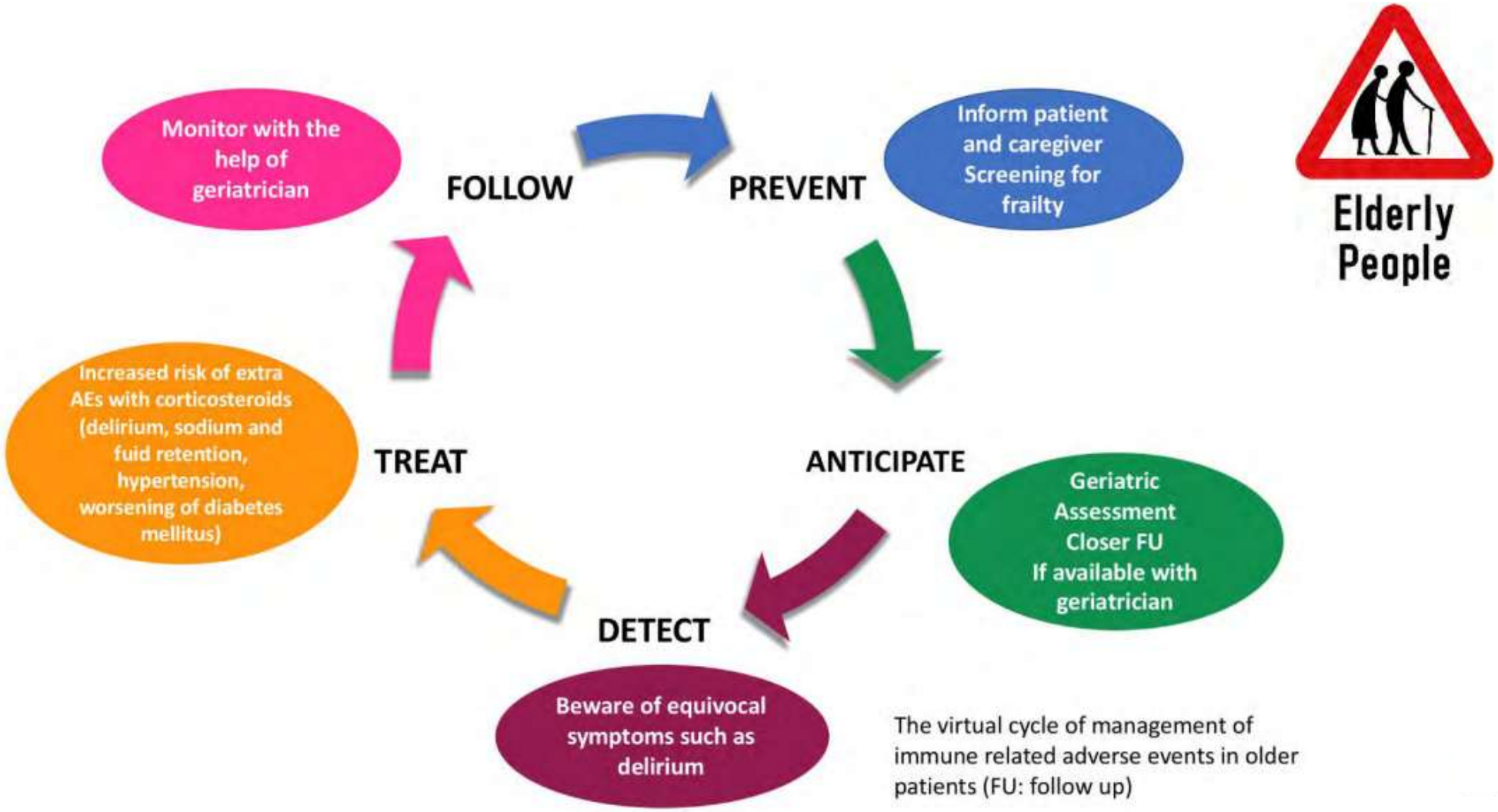
Secondary endpoints

	GAIN Arm n (%)	SoC Arm n (%)	p-value
Advanced directive completion	**278 (70%)**	**119 (59%)**	**<0.01**
ER visits for chemotox	109 (27%)	62 (31%)	0.40
Hospitalizations due to grade 3+ chemotox	88 (22%)	39 (19%)	0.43
Hospitalizations due to grade 4+ chemotox	19 (22%)	14 (36%)	0.09
Average Length of stay [median (range)]	4.8 (1-23	5 (1.7-26)	0.60

Satistically significant increase in AD completion

Daneng Li, et al. ASCO 2020 and JAMA Oncology 2021

How to prevent Toxicity in Older Patients



The virtual cycle of management of immune related adverse events in older patients (FU: follow up)

La storia di Carla

Da febbraio 2025 il paziente assume olaparib alla dose di 600 mg ridotta a maggio a una dose di 400 mg per l'anemia G2 e l'astenia G2

Gengivite G2

Non si sono verificati sintomi gastrointestinali e il paziente ha continuato a svolgere le normali funzioni quotidiane

TAC NEGATIVA

Da pochi giorni ha vinto un nuovo torneo di burraco per la sua categoria e soprattutto non rinuncerà alle sue vacanze

Conclusioni

Sì, possiamo e dobbiamo investire nelle pazienti anziane con carcinoma ovarico

Attenta selezione dei pazienti, un monitoraggio costante e l'uso di strumenti clinici appropriati, possiamo raggiungere **un equilibrio tra efficacia e sicurezza**

La terapia personalizzata e le valutazioni geriatriche aiutano a garantire che i pazienti più anziani non siano esclusi da trattamenti efficaci, ma siano invece guidati attraverso un percorso che rispetta la loro individualità, preserva la funzione e ottimizza i risultati

La medicina è un gioco di squadra: se giochiamo le carte giuste, possiamo cambiare il corso della sopravvivenza anche nella popolazione anziana