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EA2186 - A Randomized Phase II Study of Gemcitabine and Nab-Paclitaxel Compared with 5 Fluorouracil and Liposomal Irinotecan in Older Patients with Treatment Naïve Metastatic Pancreatic Cancer (***GIANT***)

NAS virtual workshop
Improving the Evidence Base for Treatment Decision-Making for Older Adults with Cancer

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Trials enrollment of older patient

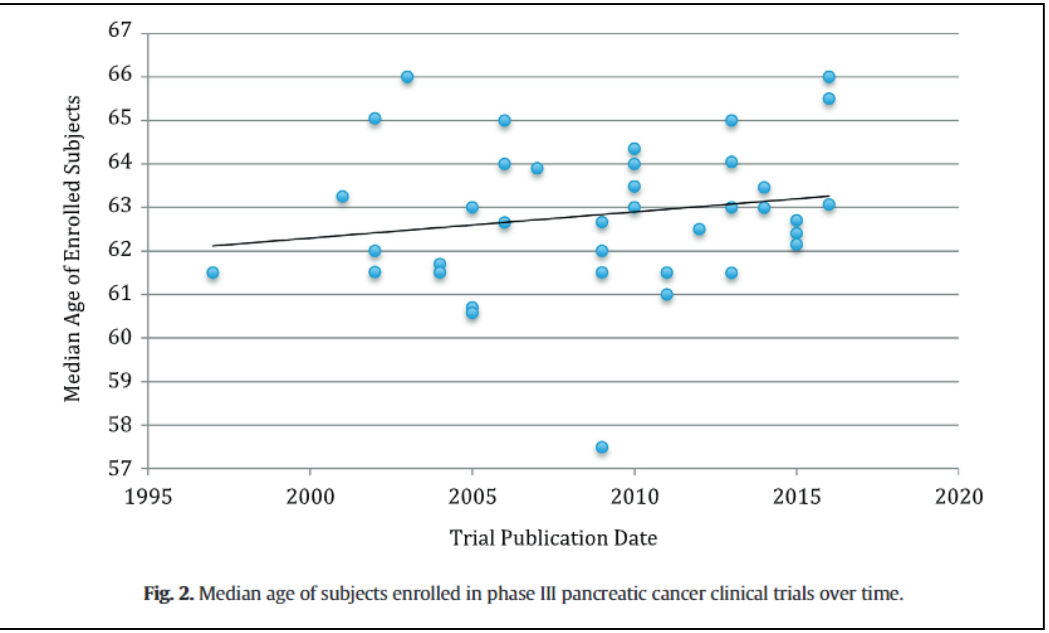
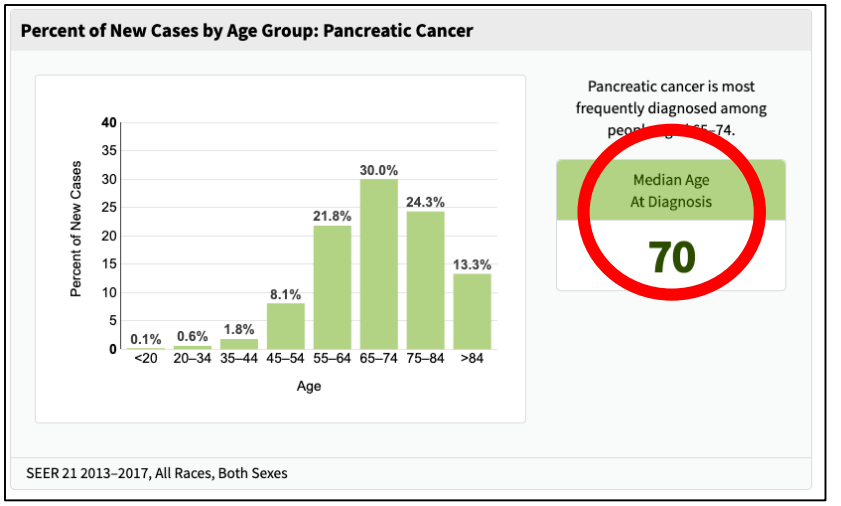
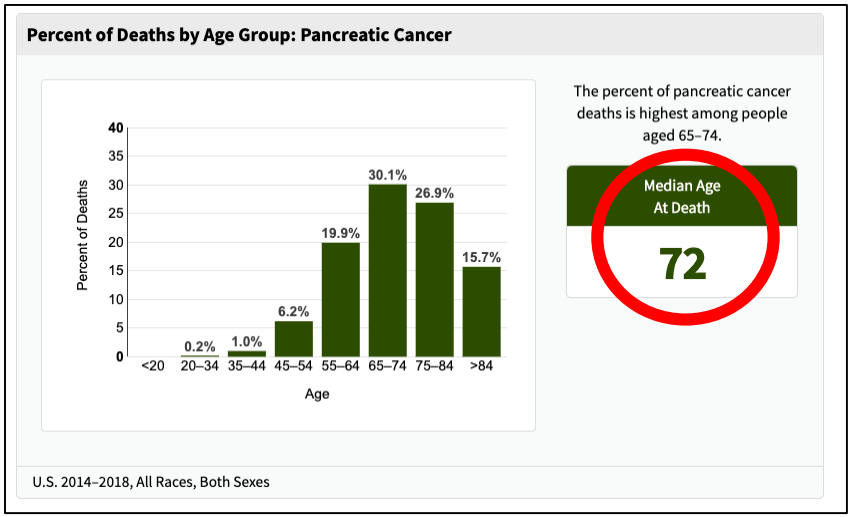


Fig. 2. Median age of subjects enrolled in phase III pancreatic cancer clinical trials over time.





White and Dotan JGO 2018

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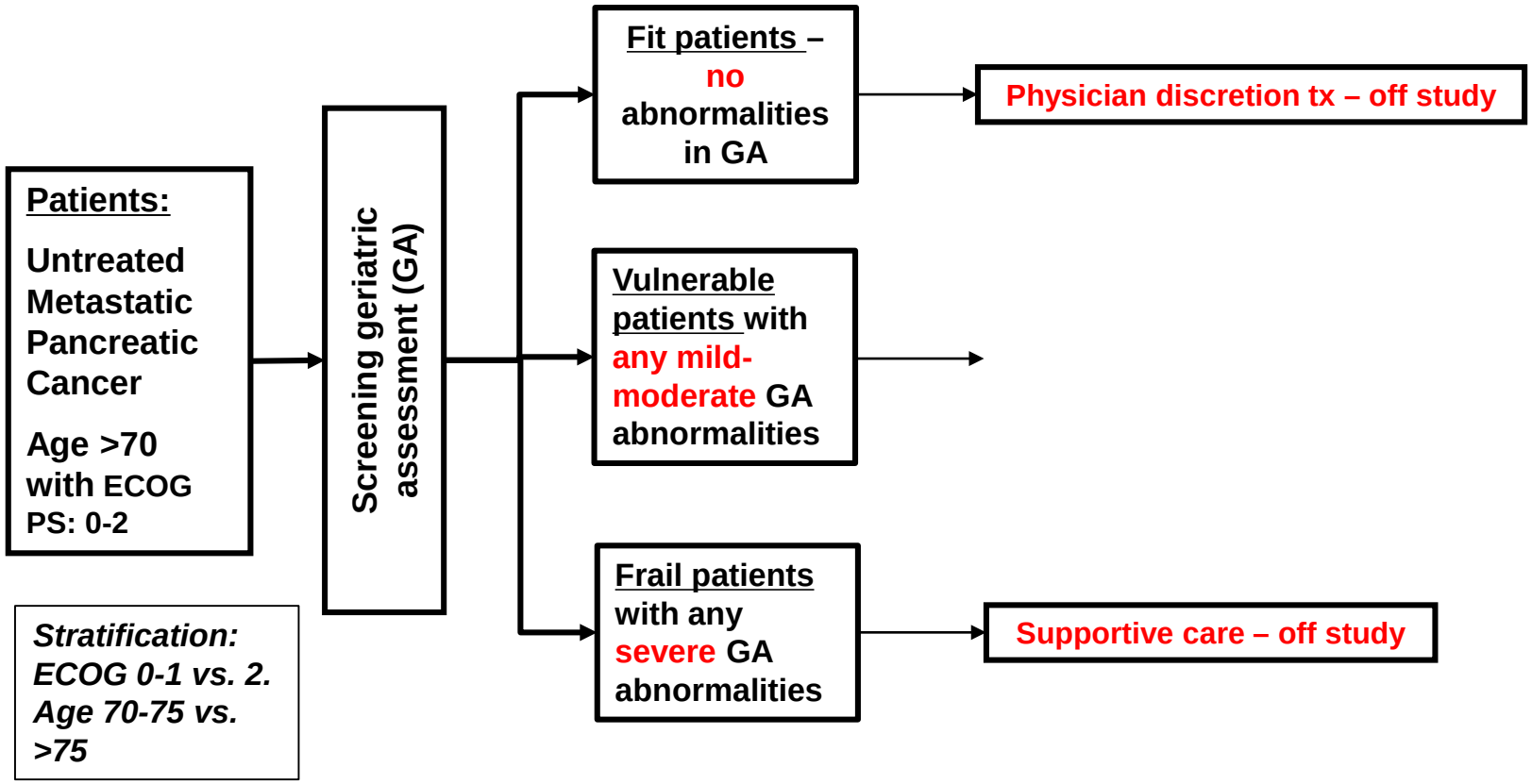
Study Rationale

- Study the “real-world” patient that is commonly seen in practice but not included in clinical trials.
- Obtain baseline data of efficacy and tolerability of front line combination chemotherapy for older patients with mPCA.
- Evaluate geriatric factors and biomarkers of aging as predictors of treatment response and tolerance in older adults with mPCA.

EA2186 - Study Design Randomized Phase II



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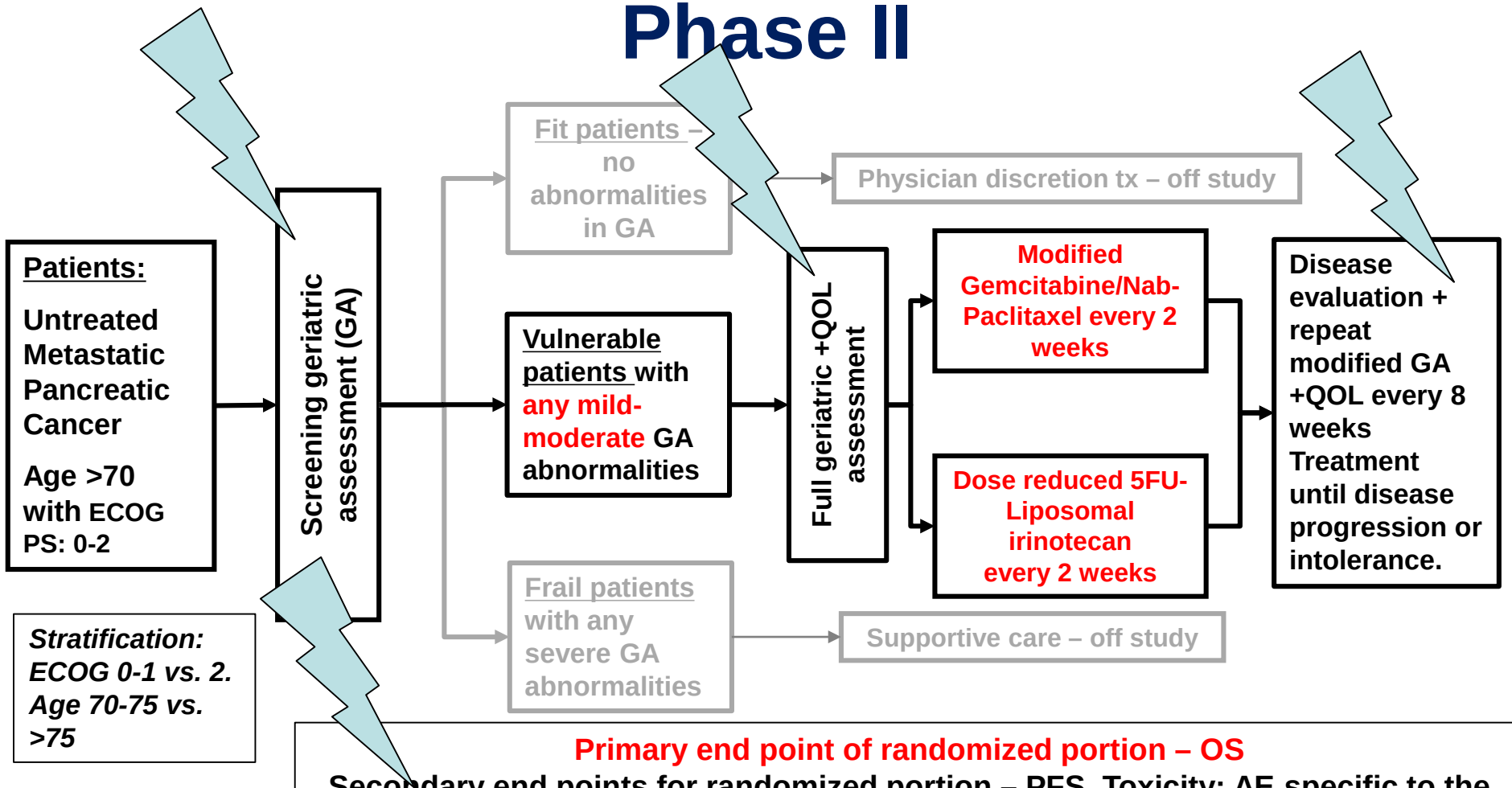
EA2186 - Study Design Randomized Phase II



Primary end point of randomized portion – OS

Secondary end points for randomized portion – PFS, Toxicity; AE specific to the older adults.

Exploratory end point – Sarcopenia, biomarkers of aging

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Eligibility:

Open eligibility to ensure accrual of real world patients!

- **Newly diagnosed metastatic pancreatic cancer**
- **>70 year old with ECOG 0-2**
- **Adequate organ function (hematologic, hepatic, renal)**
- **Ability to understand and provide informed consent**
- **Score vulnerable on screening geriatric assessment**

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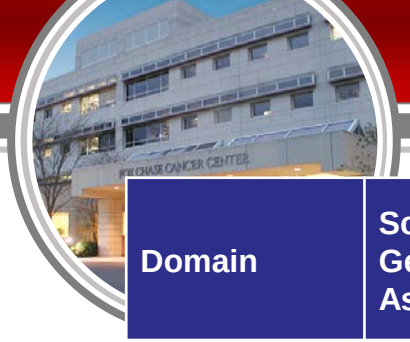

Domain	Screening Geriatric Assessment	Fit - no GA abnormalities	Vulnerable- any mild-moderate GA abnormalities	Frail- any severe GA abnormalities
Functional status[1]	ADL IADL	6 8F/5M	5 6-7F/4M	≤4 <5F/≤3M
Co-morbidities[2]	CIRS-G	No score 3-4 AND <5 comorbidities with a score of 2	No score 3-4 AND <8 comorbidities with a score of 2	>=1 score 3-4 OR >8 comorbidities with a score of 2
Cognition[3]	Blessed Orientation Memory Concentration Test	0-4	5-10	≥11
Age[2]*			≥80	
Geriatric Syndromes[4]	• Repeated Falls (>3 in 6m) • Urinary/Fecal incontinence	None	None	Presence of any of these would exclude patients

[1]Corre et al. JCO 2016 [2]Tucci et al; Leukemia and Lymphoma 2015. [3] Mohile et al; JCO 2018. [4]GrantPax study - Betge et al. BMC 2018

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Geriatric /QOL Assessment Tools	Assessment	Administered by	Assessment timing	
			Pre-tx	Disease evaluation
Activities of Daily Living subscale (ADL)	Functional status	Patient	X	X
ECOG PS		MD	X	
Instrumental Activities of Daily Living (IADL)		Patient	X	X
# of falls in the past 6 months		CRC	X	
Cumulative Illness Rating Scale – Geriatric (CIRS-G)	Comorbidity	CRC	X	
Pre-treatment Body Mass Index (BMI)	Nutrition	CRC	X	
Weight loss over 6 months		Patient	X	
Mini Nutritional Assessment (MNA)		CRC	X	
Geriatric Depression Scale	Depression	Patient	X	
Blessed Orientation Memory Concentration Test	Cognition	CRC	X	
FACT-Hep (Version 4)	QOL	Patient	X	X
Estimated time of evaluation GA + QOL			~20 min	~5-10min

Elderly Specific Toxicities:

Any Grade 5 Toxicity	Grade 4 Toxicity	Grade 3 or higher toxicity	Elderly specific toxicities of concern
	Thrombocytopenia **Febrile neutropenia** **Infection** **Peripheral neuropathy**	**Bleeding** **Diarrhea** **Fatigue**	**Deterioration of PS** **Falls** **ER visits** **Hospitalization** **Dose reductions** **Treatment discontinuation**

Correlative studies:

1. Sarcopenia:

Determine the association of baseline CT measurements of muscle and adipose tissue with treatment tolerance, PFS and OS.

2. Biomarkers of aging: IL6, CRP, D-Dimer

Banking of peripheral blood for future studies.

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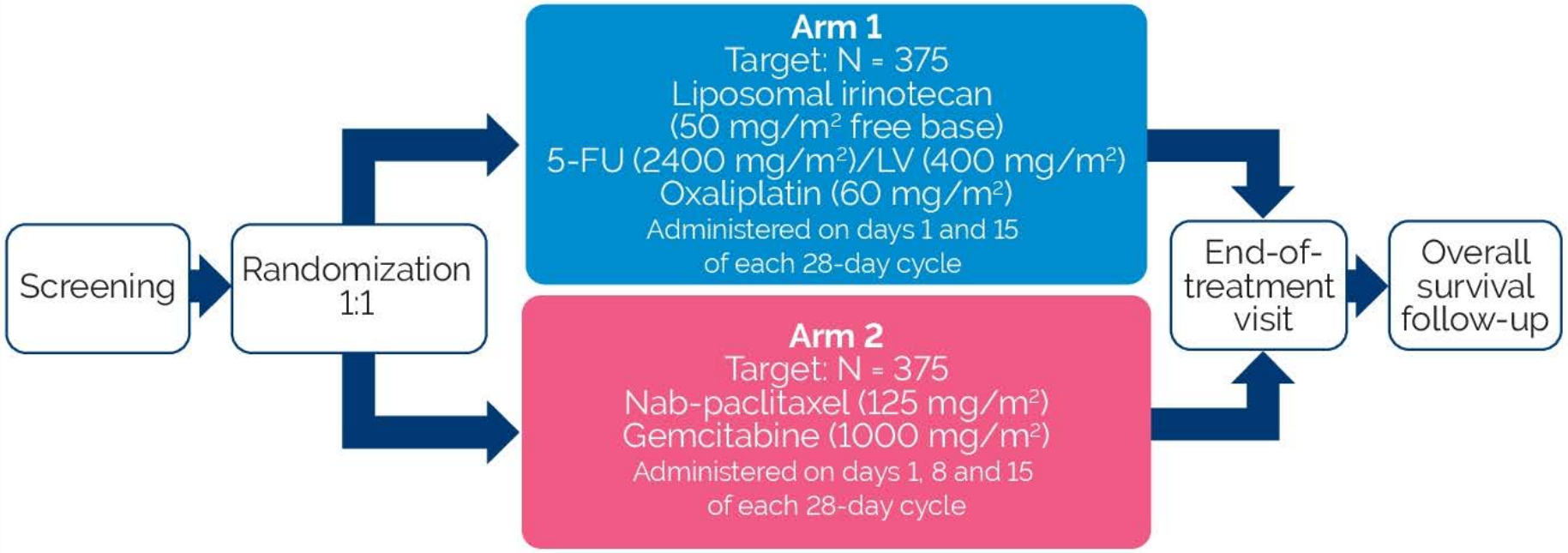
Specific considerations for elderly specific clinical trial design:

Goal	EA2186 – GIANT study
1. Patient selection	• Development of screening geriatric assessment
2. Data collection to inform care for older adults	• Conduct a full geriatric assessment • Evaluation of function through out the trial • Evaluation of QOL through out the trial • Recording of adverse events that are important for older patients
3. Eligibility criteria	• Wide eligibility to fit “real-world” patients
4. Sites	• Study is open through the cooperative group network with extensive access to community practices

Partnership with Ipsen

Ongoing Phase III front line study – Napoli3.



5-FU, 5-fluorouracil; LV, leucovorin.

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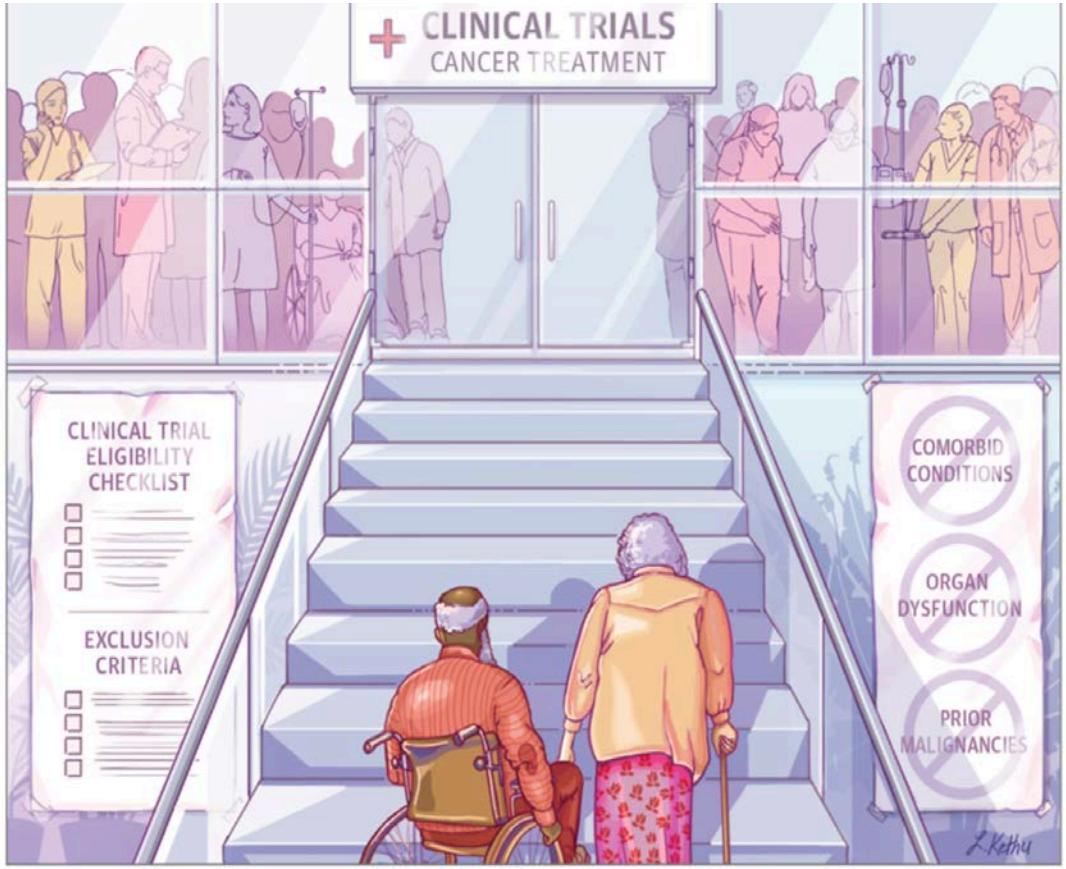
JAMA®

Medical News & Perspectives

Older Patients (Still) Left Out of Cancer Clinical Trials

Jennifer Abbasi



Abbasi et al. JAMA 2019

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