Il Suono dell'Innovazione
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La terapia di prima linea nella leucemia linfatica cronica: aspettando i dati del CLL17 all'ASH 2025

Lab of B Cell Neoplasia - Division of Experimental Oncology
Strategic Research Program on CLL –Department of Oncohematology
Università Vita-Salute San Raffaele - Milano
IRCCS Ospedale San Raffaele – Milano

Lydia Scarfò

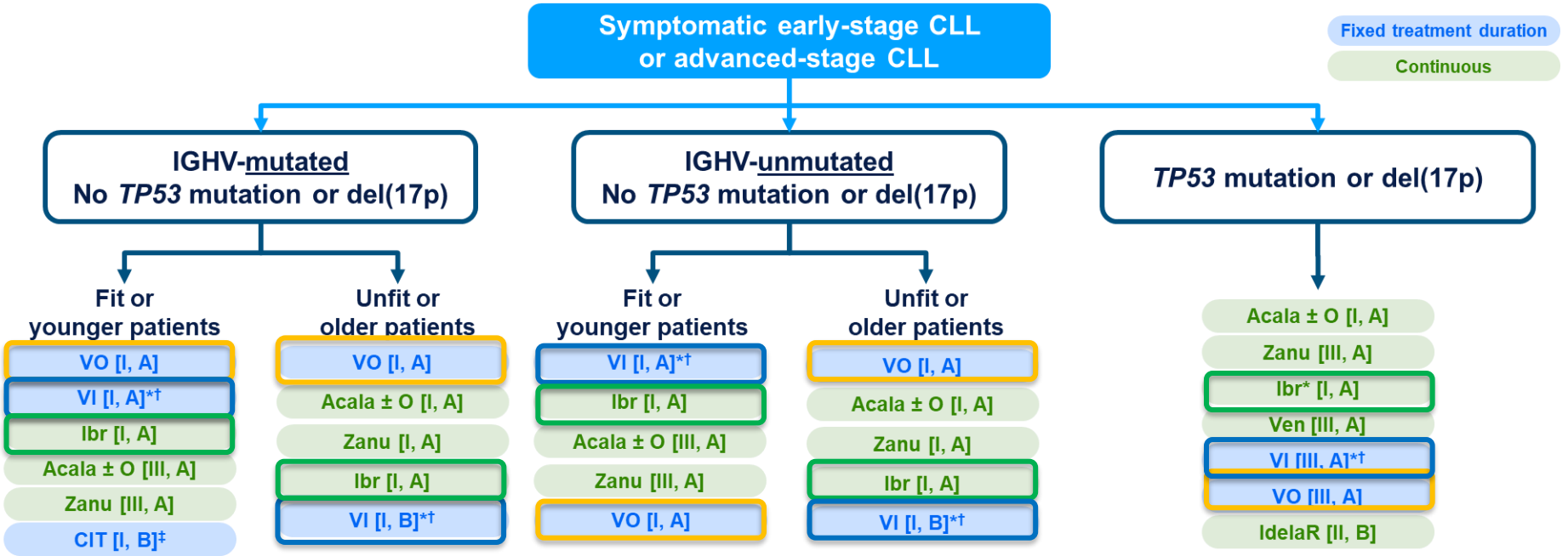
OSPEDALE
SAN RAFFAELE

UNIVERSITÀ VITA-SALUTE SAN RAFFAELE
UniSR
QUID EST HOMO?

Disclosures of Lydia Scarfò

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AbbVie			X			X	
AstraZeneca			X			X	
BeiGene			X			X	
J&J			X			X	
Lilly						X	
Merck			X				

2024 ESMO/EHA Guidelines TN CLL



When deciding between time-limited treatment vs continuous BTKi, time-limited therapy is preferred, as it is associated with reduced toxicity and retreatment would be possible at relapse

1. Eichhorst B, et al. *Ann Oncol.* 2024;**35**(9):762-768.

VO/IV/Ibrutinib: The knowledge before CLL17

Trial (Phase)	Treatment	Median age	*TP53* aberrant	ORR/CR	PFS	OS
CLL14 (3)	Venetoclax+ Obinutuzumab	72y	11.8%	84.7%/49.5%	6y-PFS 53.1%	6y-OS 78.7%
CLL13 (3)	Venetoclax+ Obinutuzumab	61y	Excluded	96.1%/56.8%	4y-PFS 81.8%	4y-OS 95.1%
CAPTIVATE-FD (2)	Ibrutinib+ Venetoclax	60y	17%	96%/55%	5.5y-PFS 60%	5.5y-OS 96%
GLOW (3)	Ibrutinib+ Venetoclax	71y	Excluded	86.8%/38.7%	5.5y-PFS 51.7%	5.5y-OS
RESONATE-2 (3)	Ibrutinib	73y	8% (TP53mut)	91%/36%	9y-PFS 50%	9y-OS 68%
ALLIANCE (3)	Ibrutinib	71y	5% del(17p) 9% TP53mut	93%/7%	4y-PFS 76%	4y-OS 85%
ECOG1912 (3)	Ibrutinib+ Rituximab	57y	0.6% del(17p)	96%/17%	5y-PFS 78%	5y-OS 95%

CLL17 Is Testing Time-Limited Targeted Combinations Versus Continuous BTKi Therapy in TN CLL

- IGHV status
- del(17p)/TP53mut
- patient fitness (CIRS)>6 and/or creatinine clearance <70 mL/min)

Patients with previously untreated CLL, including fit and unfit patients and patients with del(17p)/*TP53*

(N = 909)

R
1:1:1

Ibrutinib until intolerance or PD (n = 301)

VenG
(6 x VenG, 6 x venetoclax) (n = 303)

I+V
(3 x ibrutinib, 12 x venetoclax + ibrutinib) (n = 305)

- **Primary endpoint:** PFS (non-inferiority VO vs I and VI vs I)
- **Key secondary endpoints:** response, MRD, and OS

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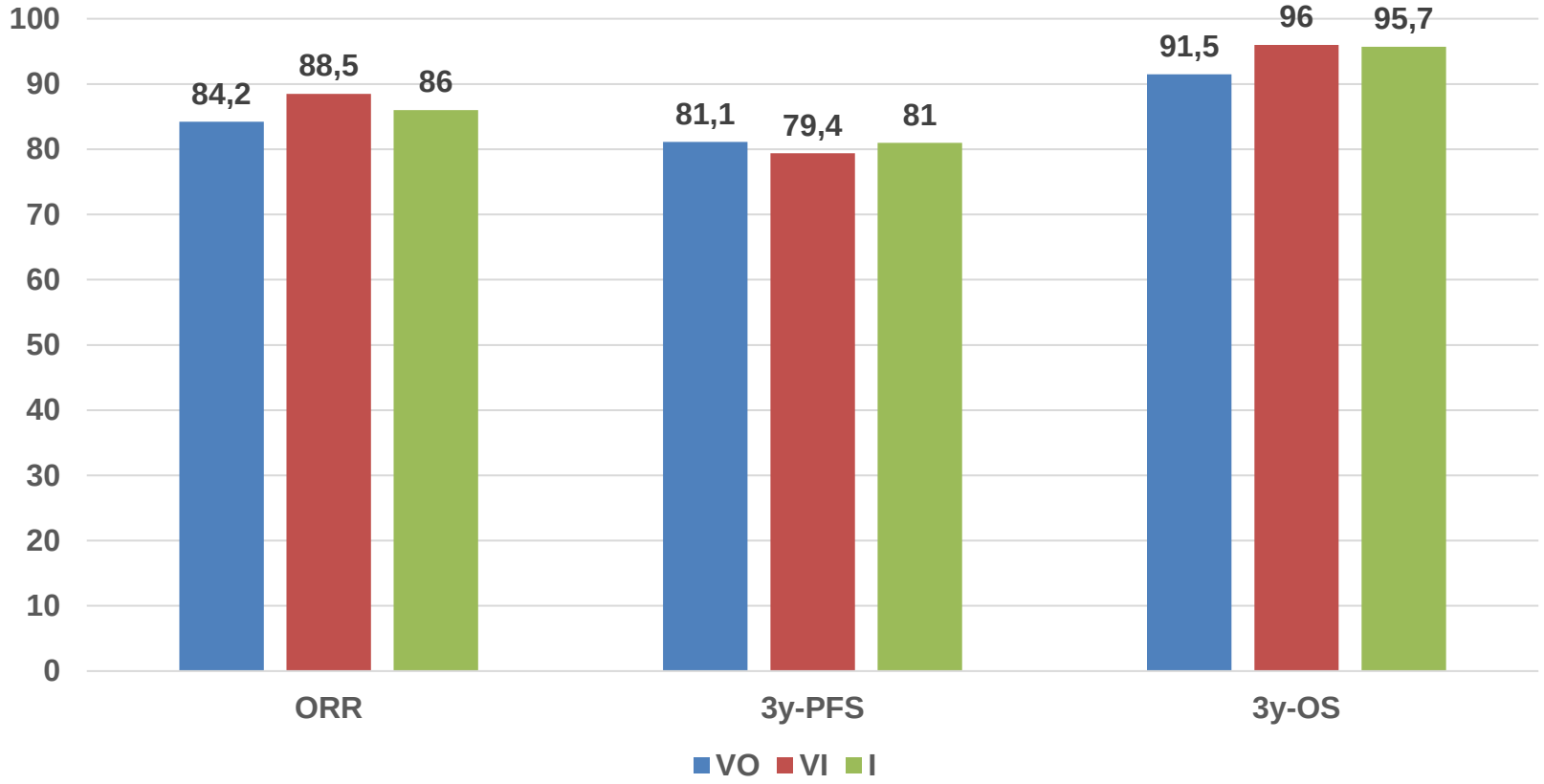

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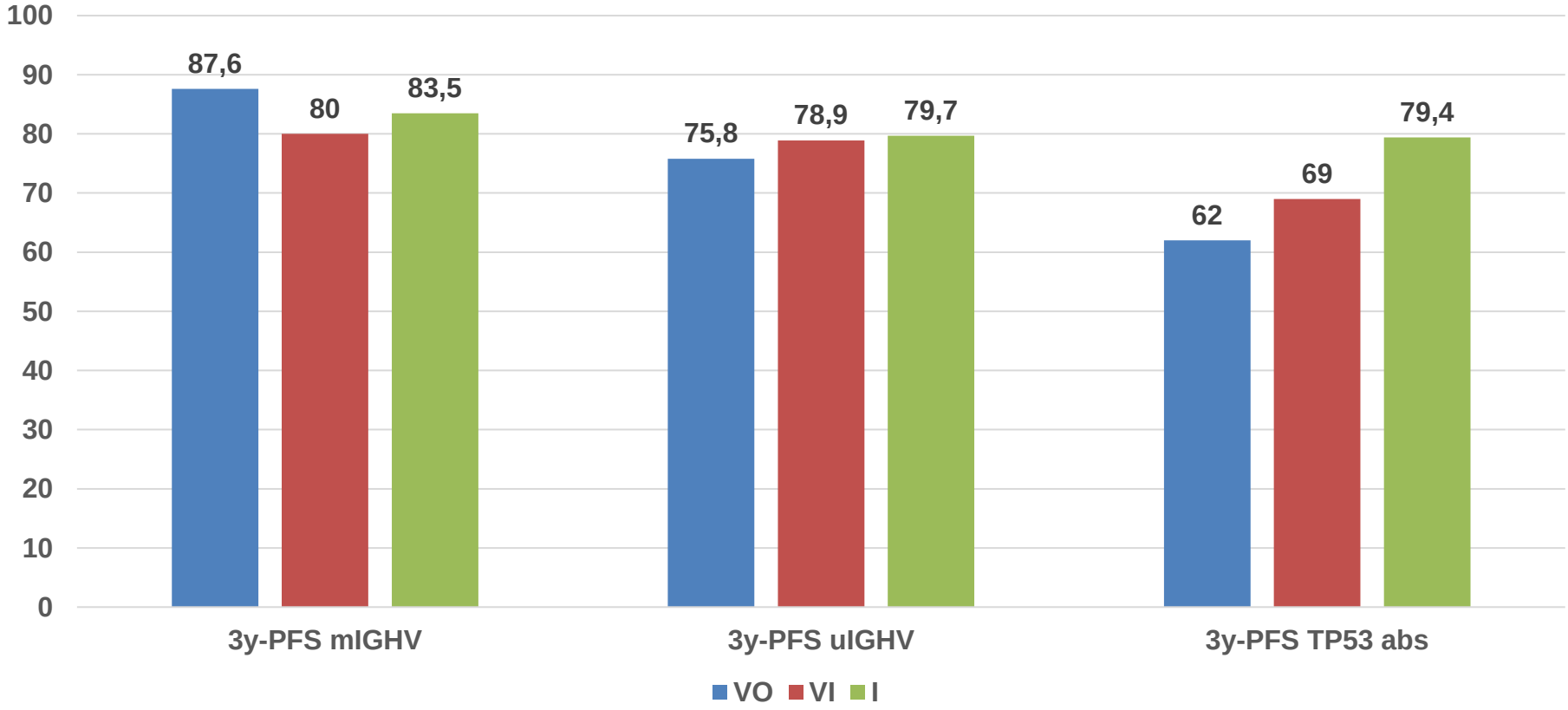

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CLL17 Safety: Most frequent AE and AESI

AE Category	VO (%)	VI (%)	I (%)
Infections and infestations	76.3	80.2	79.9
Gastrointestinal disorders	59.0	42.9	28.5
COVID-19	38.2	42.2	39.3
Cardiac disorders	13.9	23.8	34.6
Second cancers	11.5	11.2	18.5

Al-Sawaf O et al, ASH 2025

Polling question: qual è il tuo principale take home message dai dati del CLL17 in attesa della presentazione orale all'ASH2025?

1. Venetoclax + obinutuzumab per tutti tranne *TP53* aberranti
2. Ibrutinib + venetoclax per tutti inclusi i *TP53* aberranti
3. cBTKi continuativo rimane lo standard di cura nei pazienti *TP53* aberranti
4. Questi dati sono già vecchi e non ci aiutano nel panorama terapeutico attuale (acala+venetoclax ≠ ibrutinib + venetoclax, acalabrutinib o zanubrutinib ≠ ibrutinib)