Nuove prospettive nel

# MIELOMA MULTIPLO

**NAPOLI** Royal Hotel Continental

**7-8 MARZO 2022**

## Real World Evidence

Giuseppe Mele
U.O.C. di Ematologia
P.O. Antonio Perrino - Brindisi

# RETE EMATOLOGICA PUGLIESE (REP)

Ematologia, Osp. A. Perrino, Brindisi

Ematologia, Casa Sollievo della Sofferenza, San Giovanni Rotondo

Ematologia, Università degli Studi, Policlinico, Bari

Ematologia, Osp. Giovanni Paolo II°, Bari

Ematologia, Osp. Monsignor R. Dimiccoli, Barletta

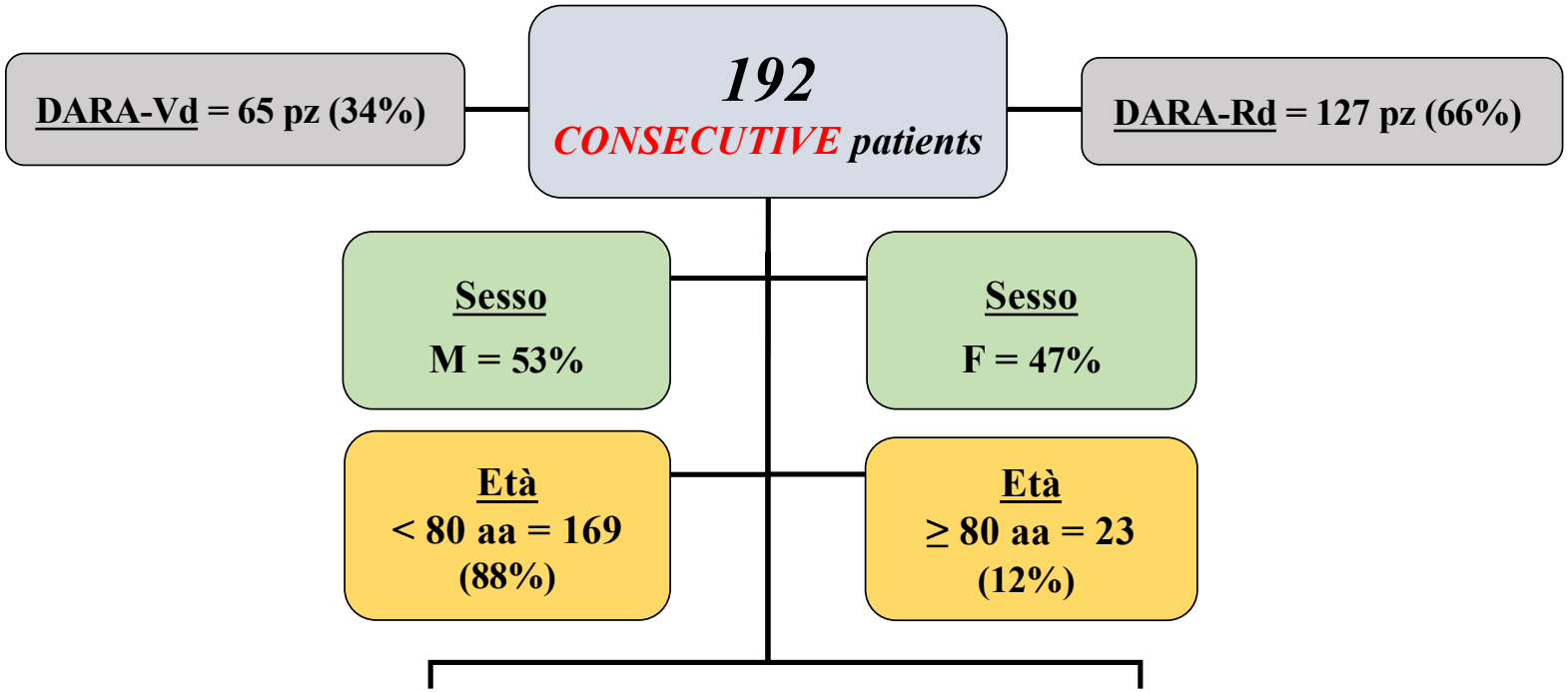
Ematologia, Ospedali Riuniti, Foggia

Ematologia, Osp. V. Fazzi, Lecce

Ematologia, Osp. G. Moscati, Taranto

Ematologia, Osp. Cardinale Panico, Tricase


Nuove prospettive nel MIELOMA MULTIPLO




***CRITERI di INCLUSIONE***

- ANC ≤ 1.0 x $10^3$/µL
- platelet count ≤ 20 x $10^3$/µL
- CrCl ≤ 30 mL/min (formula di Cockroft-Gault)
- lenalidomide-refractory patients
- patients previously treated with IMIDs
- patients previously treated with PIs
- patients with higher comorbidity burden

Nuove prospettive nel MIELOMA MULTIPLO

| Baseline Clinical Characteristics | | |
|---|---|---|
| *n. Totale Pazienti* | 192 | |

| | «DARA-Vd» | «DARA-Rd» | *P* |
|---|---|---|---|
| n. Pazienti per gruppo | 65 | 127 | |
| Età alla diagnosi MM (range) | 62,5 aa (36-81) | 66 aa (32-83) | *p* = ns |
| Età inizio «DARA» (range)<br>• < 80 aa<br>• ≥ 80 aa | 68,1 aa (40-81)<br>• 84,6% (55 pz)<br>• 15,4% (10 pz) | 70,2 aa (41-85)<br>• 90%(114pz)<br>• 10% (13 pz) | *p* = ns |
| «DARA» Timing (range) | 4 aa (0-16) | 3 aa (0-19) | |

Nuove prospettive nel MIELOMA MULTIPLO

# Clinical Presenting Characteristics (1°)

*Stadio di Malattia* (popolazione totale)

- Recidivati = 75,5% (145 pazienti)
- Refrattari = 24,5% (47 pazienti)

***«DARA-Vd group»***

- Recidivati = 80% (52 pz)
  - 1° Recidiva = 26,1% (13 pz)
  - ≥2° Recidiva = 73,9% (39 pz)
- Refrattari = 20% (13 pz)

***«DARA-Rd group»***

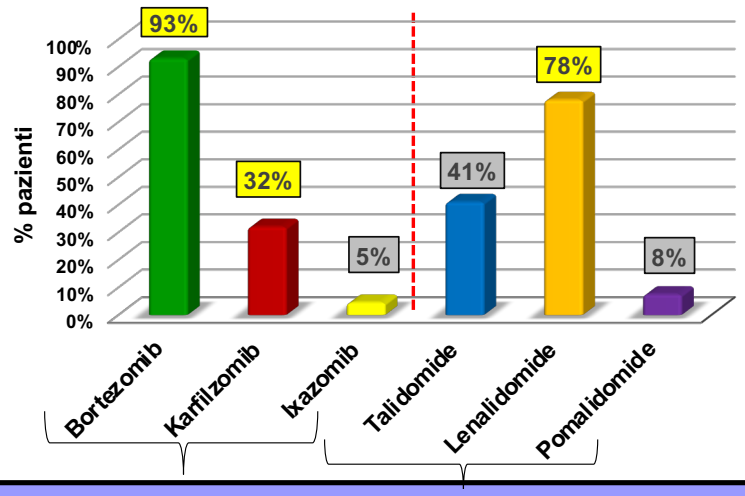
- Recidivati = 73,2% (93 pz)
  - 1° Recidiva = 80,3% (70 pz)
  - ≥2° Recidiva = 19,7% (23 pz)
- Refrattari = 26,8% (34 pz)

| Clinical Presenting Characteristics (2°) - ISS | | |
|---|---|---|
| "DARA-Vd group" (n. 65 pazienti) | I° = 55%<br>II° = 16%<br>III° = 29% | *p* = ns |
| "DARA-Rd group" (n. 127 pazienti) | I° = 55%<br>II° = 24%<br>III° = 21% | |

| Dettagli DARA-Vd | |
|---|---|
| *n. linee di trattamento precedenti* | **2 (range 1-6)**<br>• **26,1% (17 pz) = dopo 1 linea di trattamento**<br>• **73,9% (48 pz) = dopo ≥2 linea di trattamento**<br>- dopo 2 linee di trattamento = 41,7% (20 pz)<br>- dopo ≥3 linee di trattamento = 58,3% (28 pz) |

| Dettagli DARA-Rd | |
|---|---|
| *n. linee di trattamento precedenti* | **1 (range 1-4)**<br>• **80,3% (102 pz) = dopo 1 linea di trattamento**<br>• **19,7% (25 pz) = dopo ≥2 linea di trattamento**<br>- dopo 2 linee di trattamento = 72% (18 pz)<br>- dopo ≥3 linee di trattamento = 28% (7 pz) |

## Dettagli sui Precedenti Trattamenti in Dara-Vd




pazienti pesantemente pretrattati

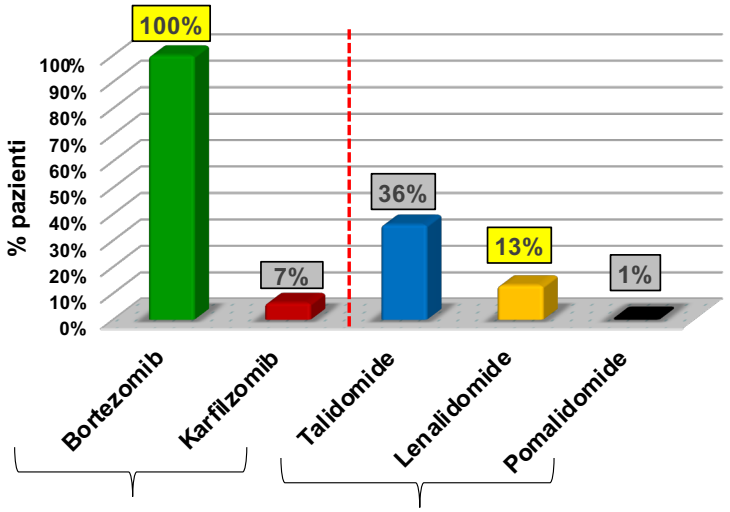
## Dettagli sui Precedenti Trattamenti in Dara-Rd

Il 95% dei pazienti sono "Lena-Refractory" =

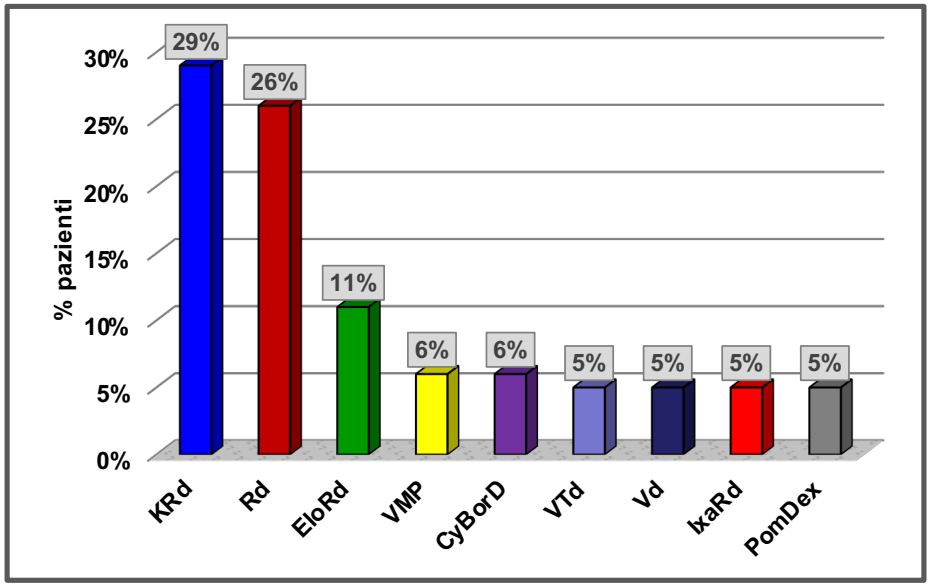
**ORRs** = 75%

(CR 25%; VGPR 19%; PR 31%)

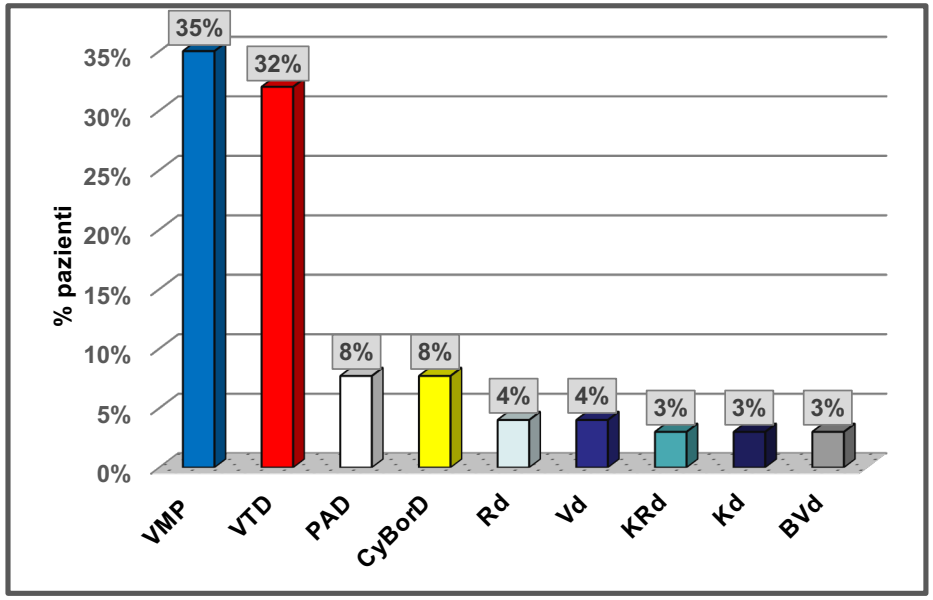
**NR** = 25%



## Ultimo Trattamento prima di Dara-Vd

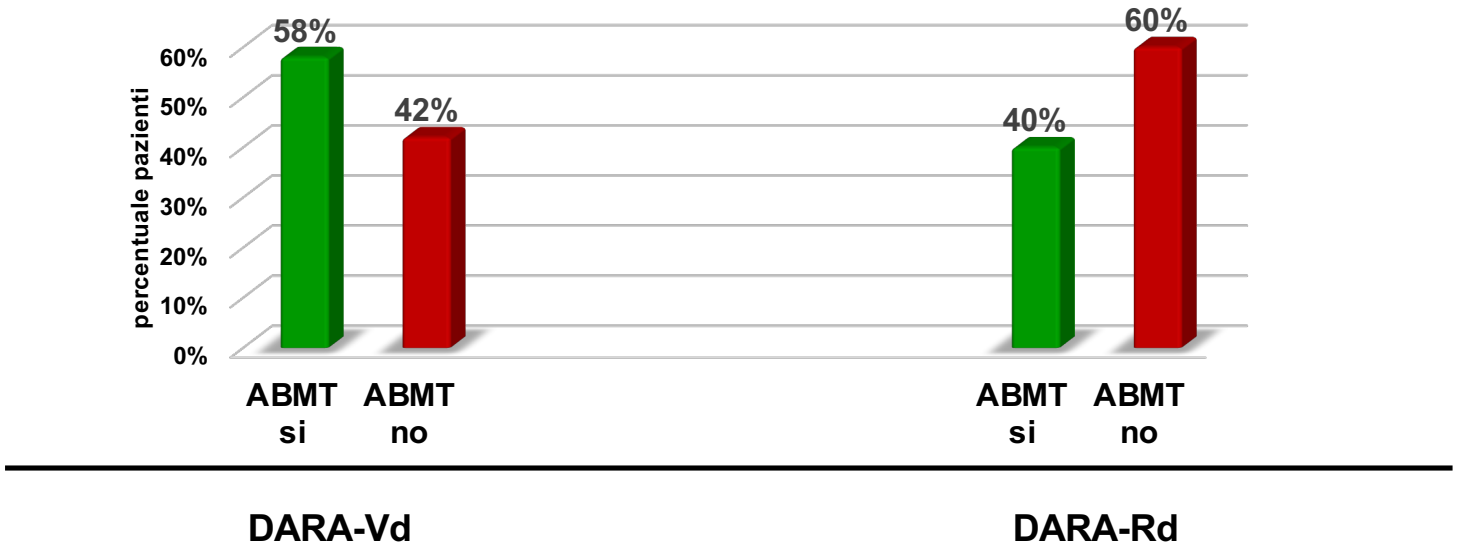



## Ultimo Trattamento prima di Dara-Rd

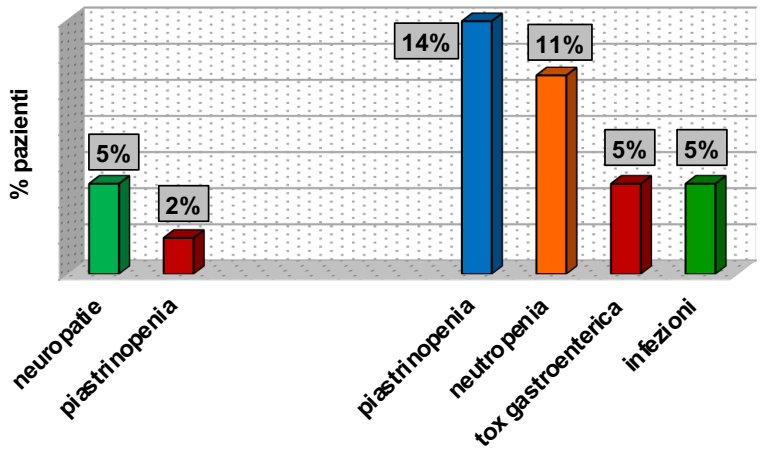


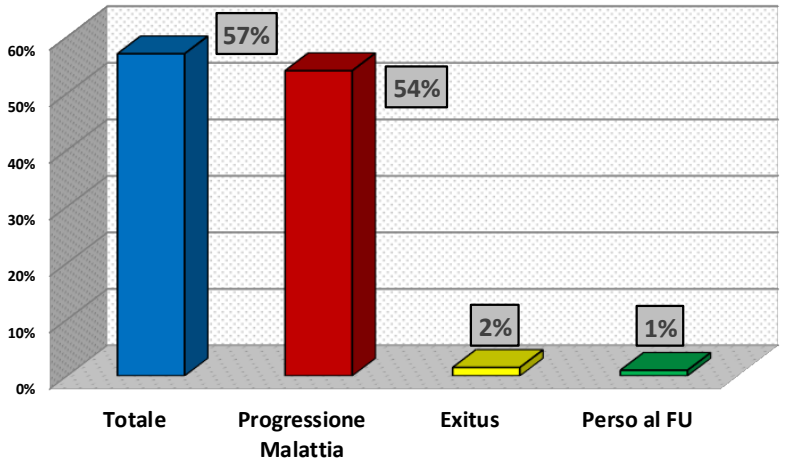

Nuove prospettive nel MIELOMA MULTIPLO

| DARA-Vd | DARA-Rd |
|---|---|
| ABMT si = 58% | ABMT si = 40% |
| ABMT no = 42% | ABMT no = 60% |



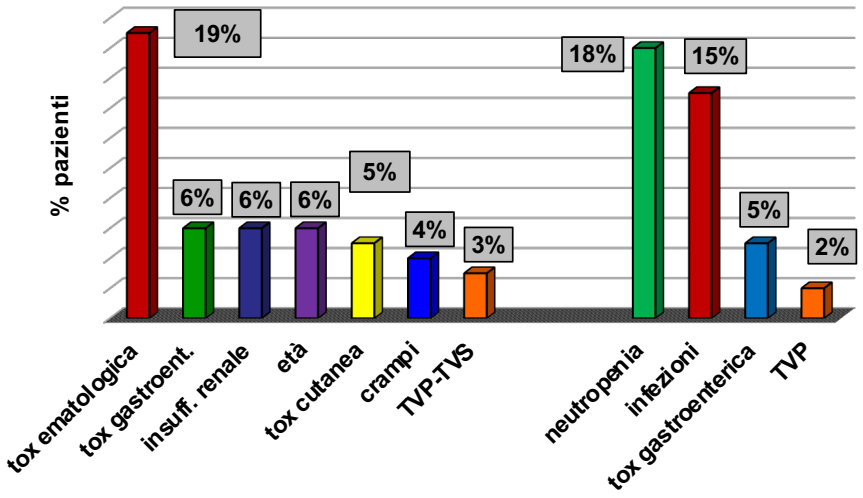
| Dettagli "DARA-Vd" | |
|---|---|
| n. cicli «Dara-Vd» (range) | 8 (1-34) |
| riduzione della dose bortezomib | 7% |
| ritardo avvio del ciclo successivo (*) | 32% |
| sospensione definitiva del trattamento | 57% |

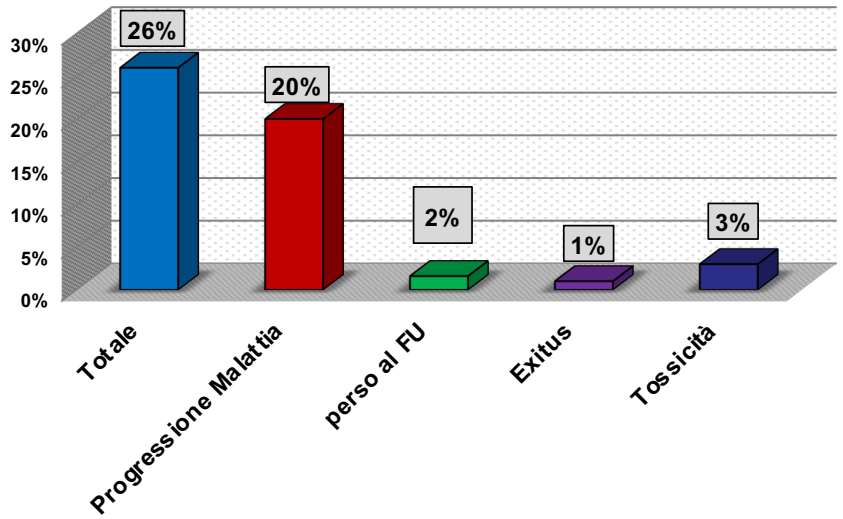



**RIDUZIONE** **RITARDO** **STOP DEFINITIVO**

| Dettagli "DARA-Rd" | |
|---|---|
| n. cicli «Dara-Rd" (range) | 12 (1-33) |
| riduzione della dose lenalidomide | 52,5% |
| ritardo avvio del ciclo successivo | 39% |
| sospensione definitiva del trattamento | 26% |

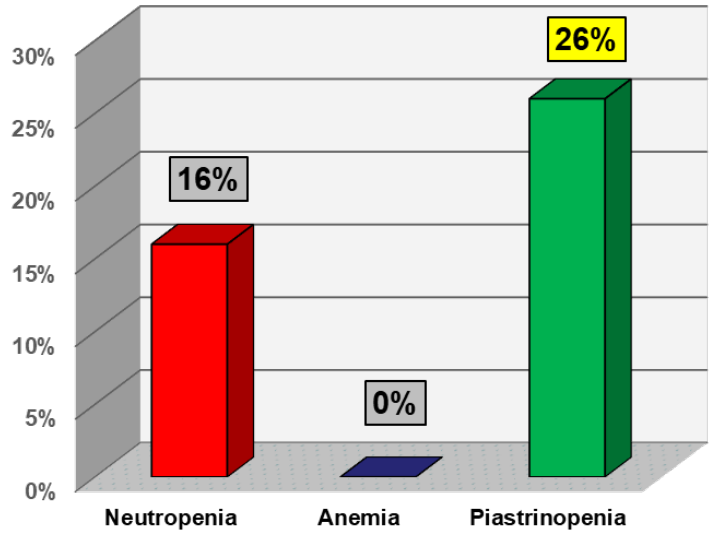


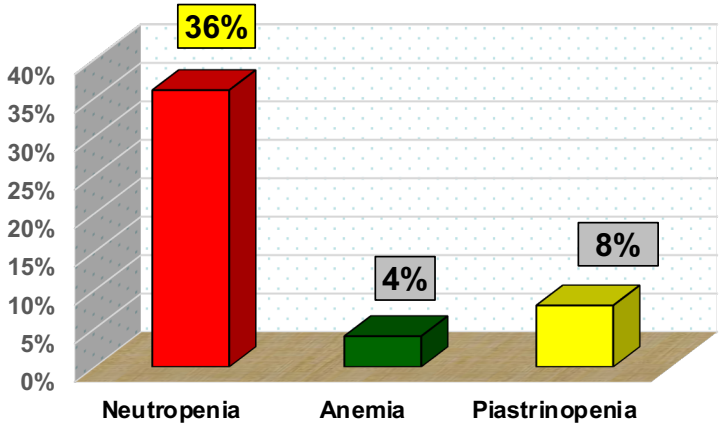




RIDUZIONE RITARDO STOP DEFINITIVO

# TOSSICITA' – follow-up a 12 mesi

- **TOSSICITA' EMATOLOGICA**
- TOSSICITA' NON-EMATOLOGICA

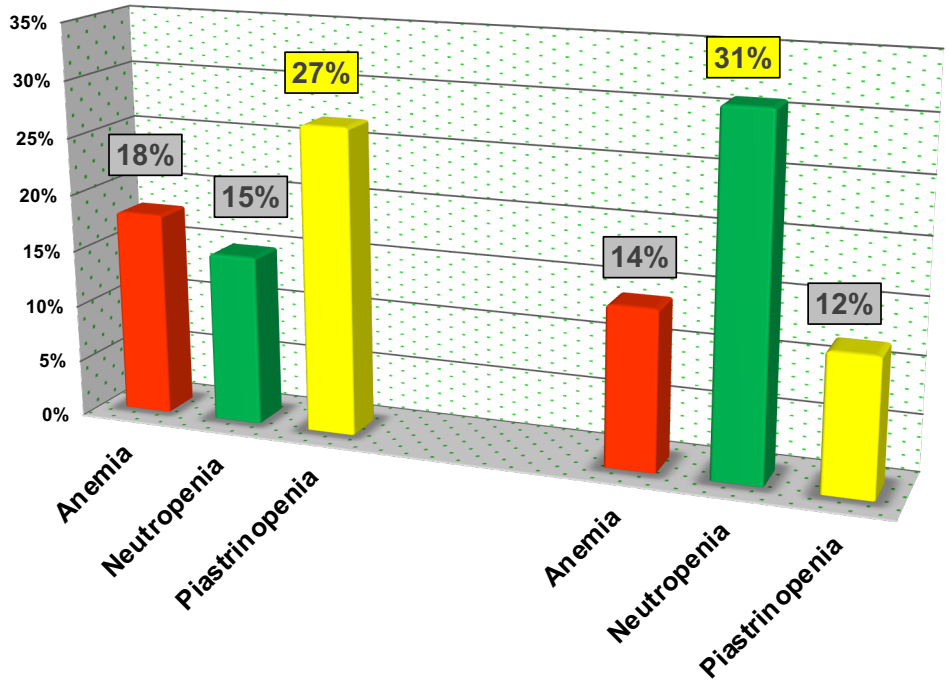



**DARA-Vd** **DARA-Rd**

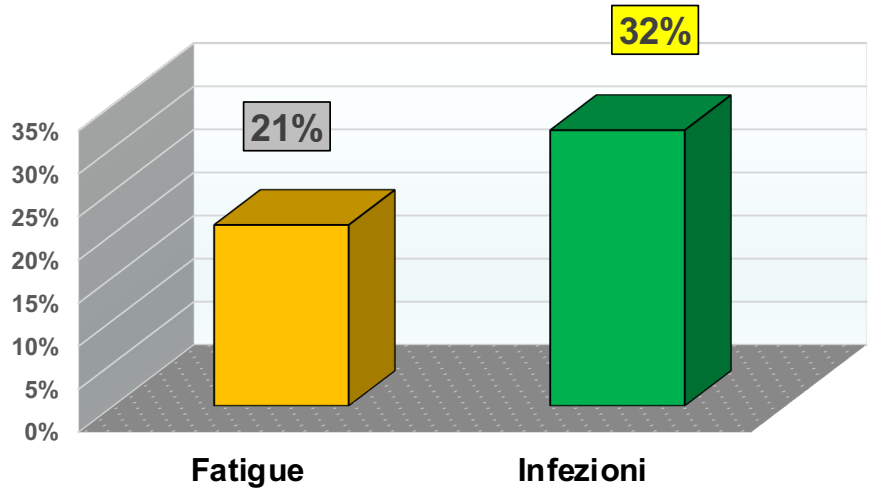
# TOSSICITA' – follow-up a 28 mesi

- **TOSSICITA' EMATOLOGICA**
- TOSSICITA' NON-EMATOLOGICA

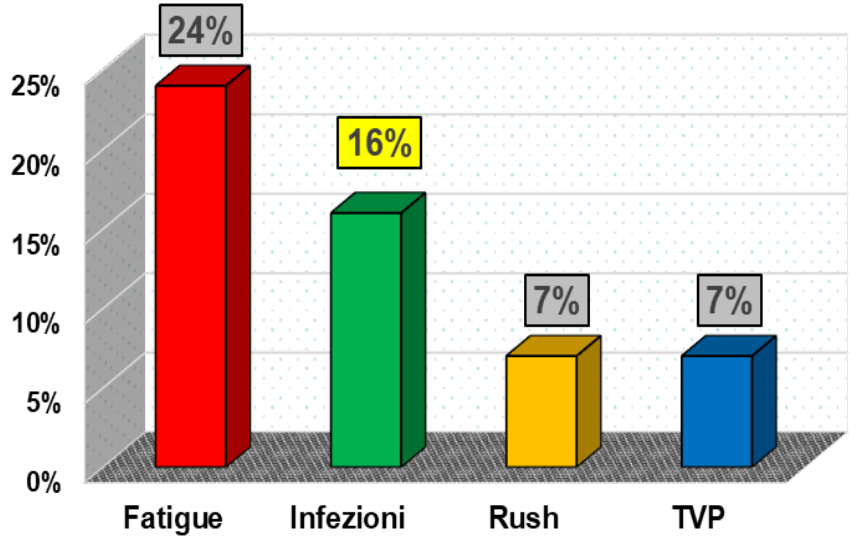


# TOSSICITA' – follow-up a 12 mesi

- TOSSICITA' EMATOLOGICA
- TOSSICITA' NON-EMATOLOGICA



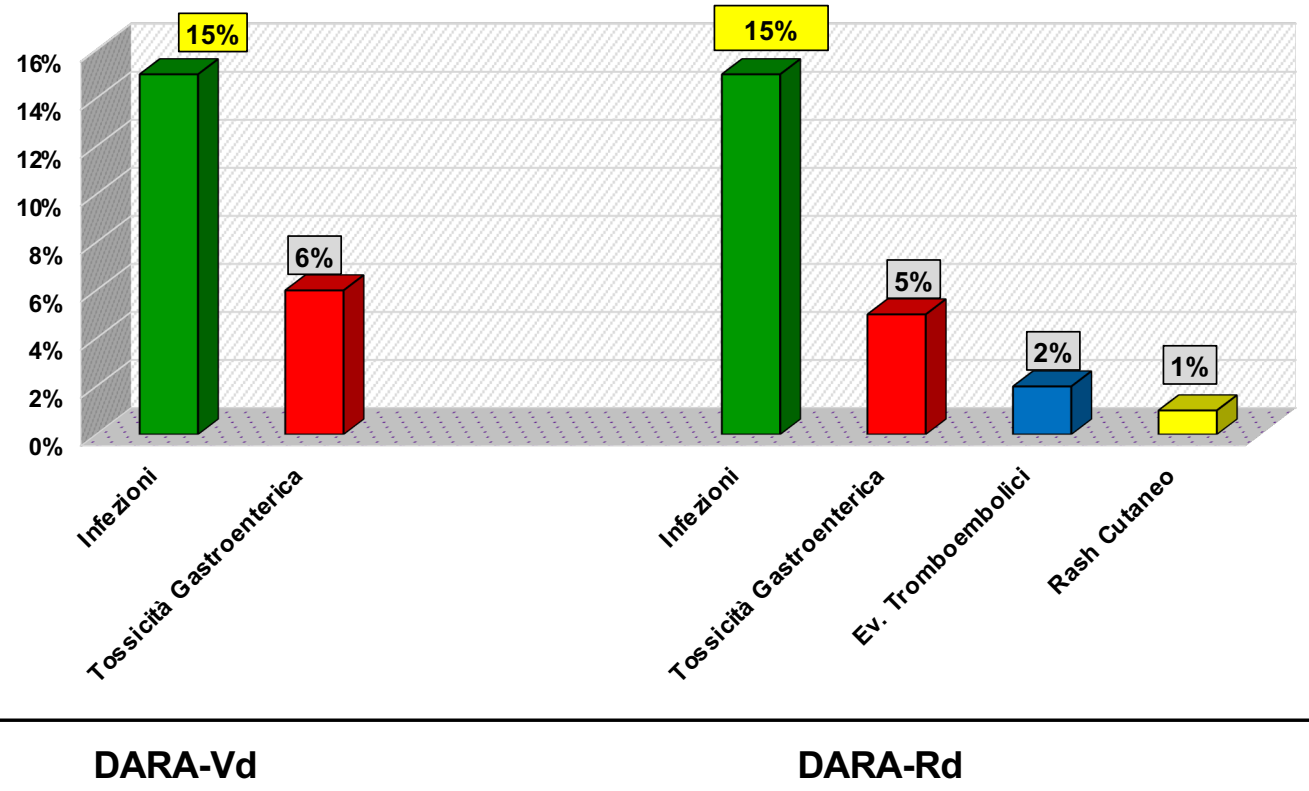

DARA-Vd

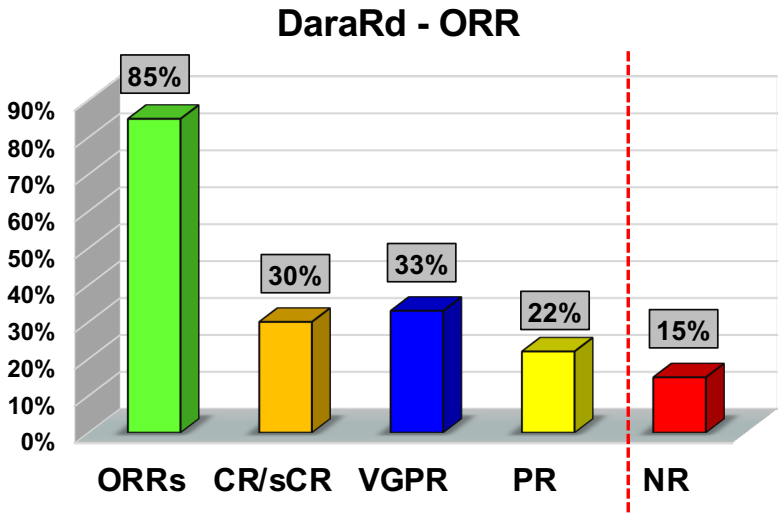



DARA-Rd

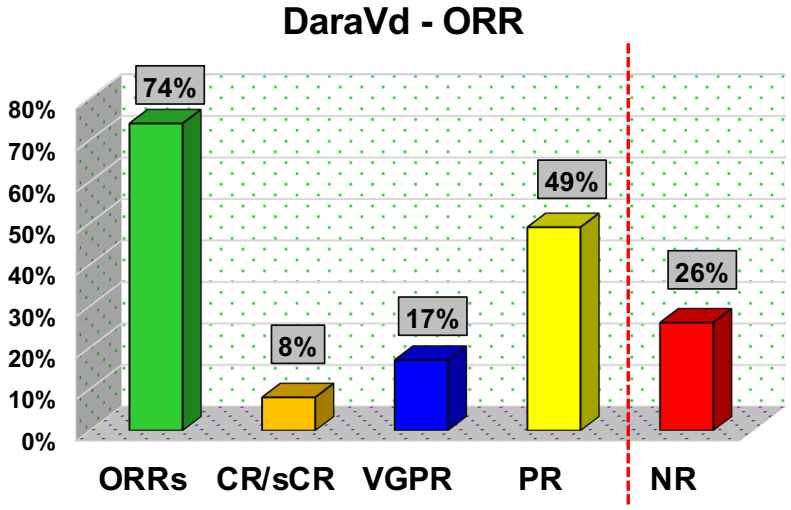
# TOSSICITA' – follow-up a 28 mesi

- TOSSICITA' EMATOLOGICA
- **TOSSICITA' NON-EMATOLOGICA**



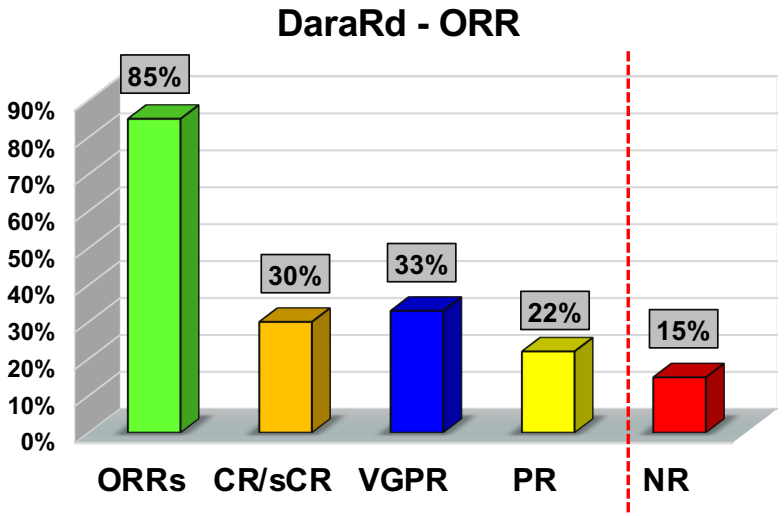


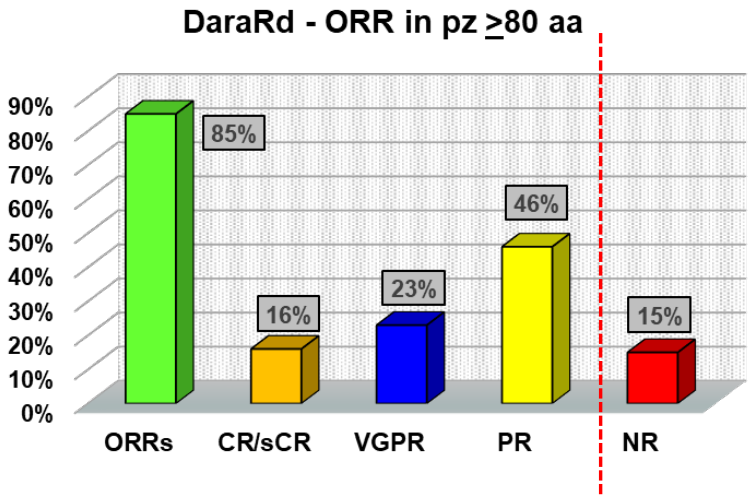

pz "prevalentemente" in 1° recidiva

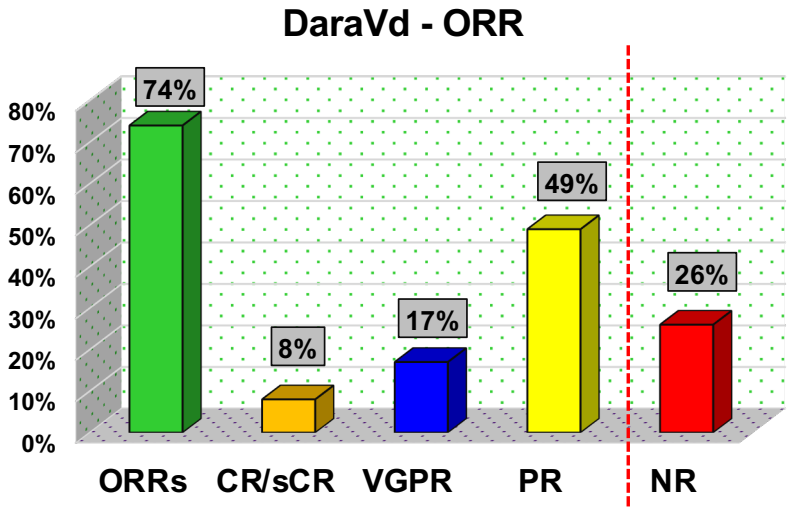


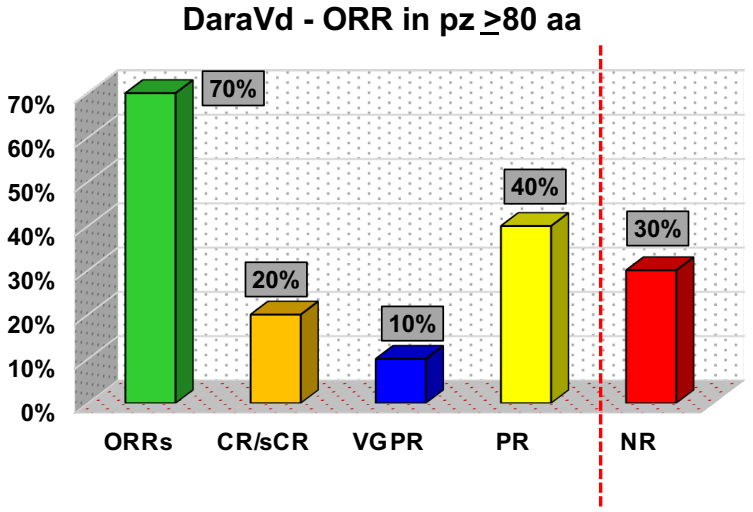

pz "prevalentemente" in ≥2° recidiva

Nuove prospettive nel MIELOMA MULTIPLO

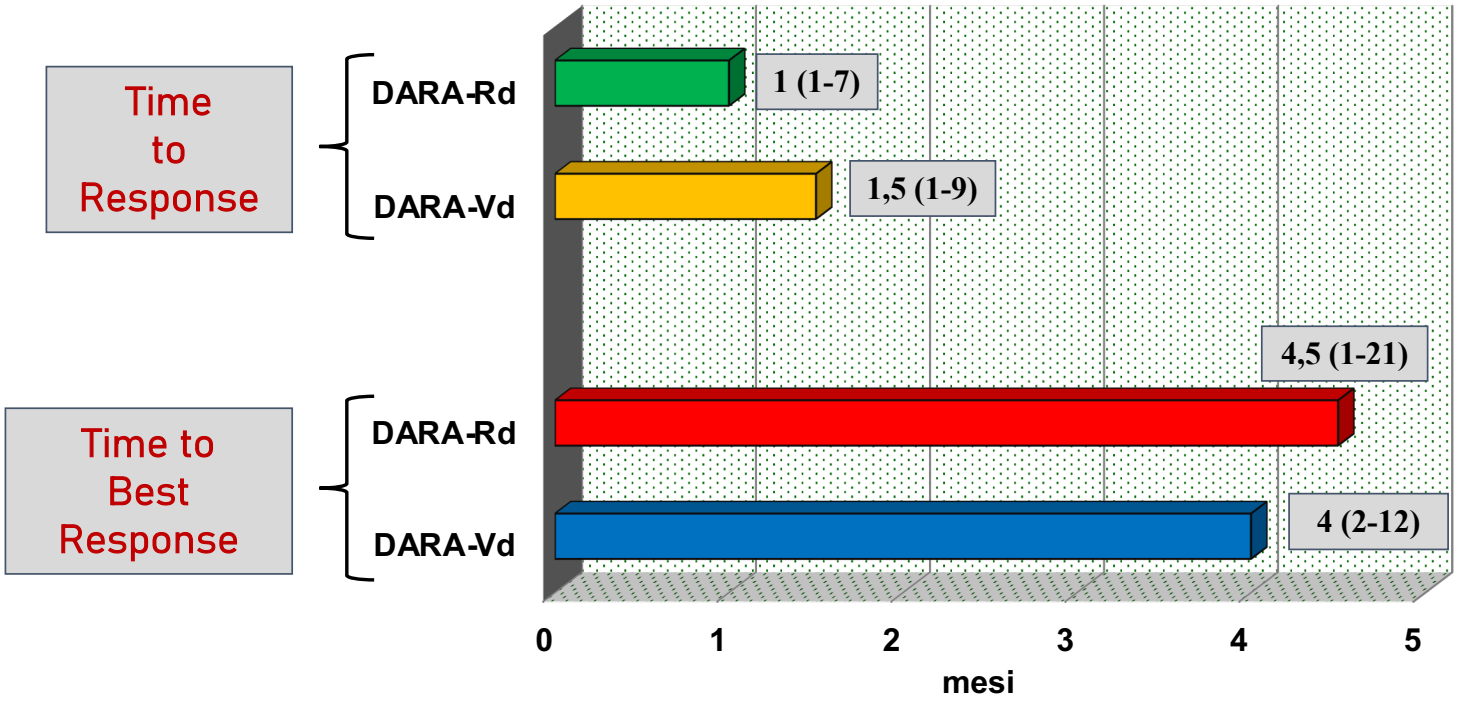

DaraRd - ORR
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
85%
30%
33%
22%
15%
ORRs
CR/sCR
VGPR
PR
NR


DaraRd - ORR in pz ≥80 aa
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
85%
16%
23%
46%
15%
ORRs
CR/sCR
VGPR
PR
NR


DaraVd - ORR
80%
70%
60%
50%
40%
30%
20%
10%
0%
74%
8%
17%
49%
26%
ORRs
CR/sCR
VGPR
PR
NR

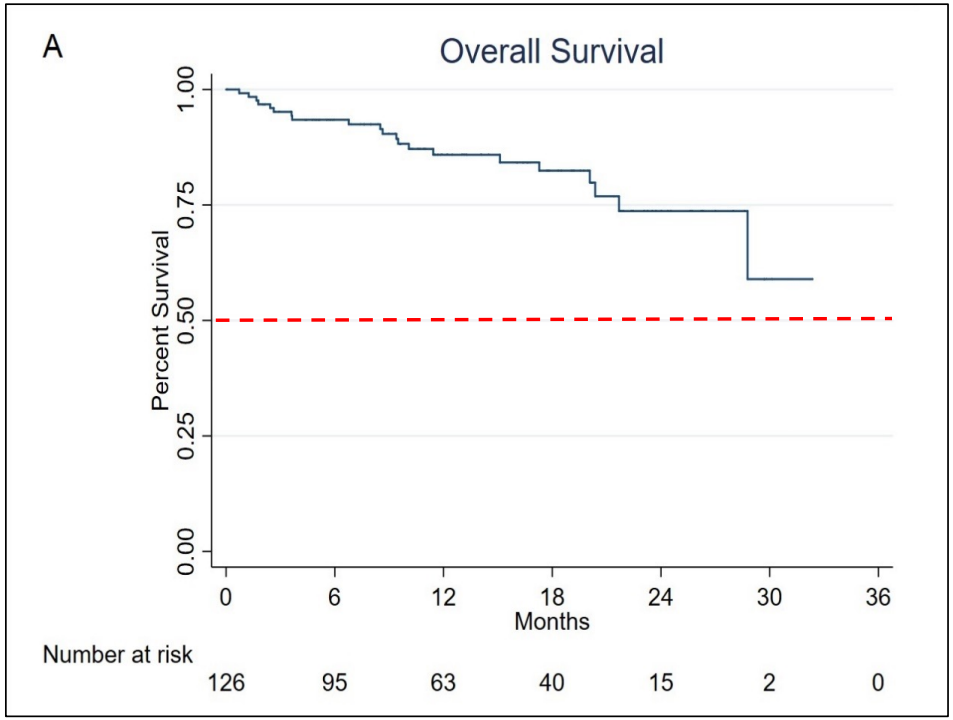

DaraVd - ORR in pz ≥80 aa
70%
60%
50%
40%
30%
20%
10%
0%
70%
20%
10%
40%
30%
ORRs
CR/sCR
VGPR
PR
NR

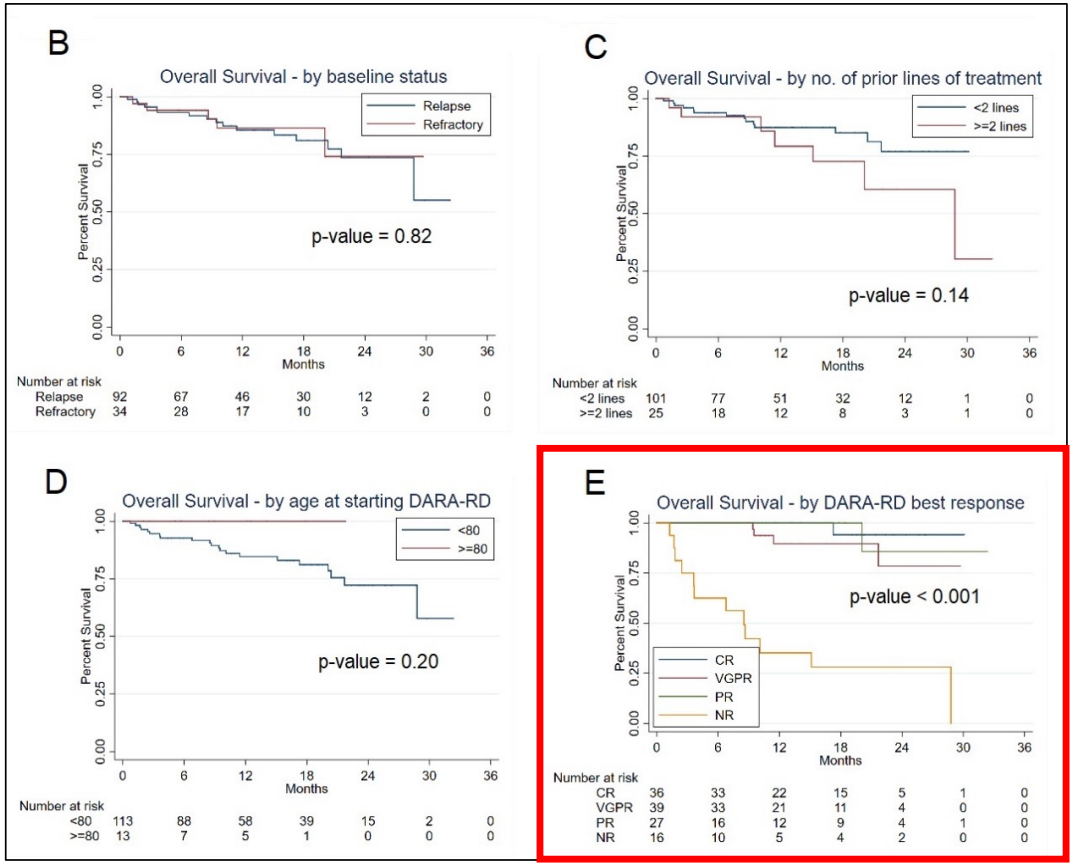
# Efficacy Endpoints




Nuove prospettive nel MIELOMA MULTIPLO

**Overall Survival** in a cohort of Multiple Myeloma patients treated with **D-Rd** (Panel A) and in subgroups of patients according to baseline status of relapse/refractory (Panel B), prior line of treatment (<2 vs ≥2) (Panel C), age at starting DRd treatment (<80 vs ≥80) (Panel D) and best response to treatment (Panel E)

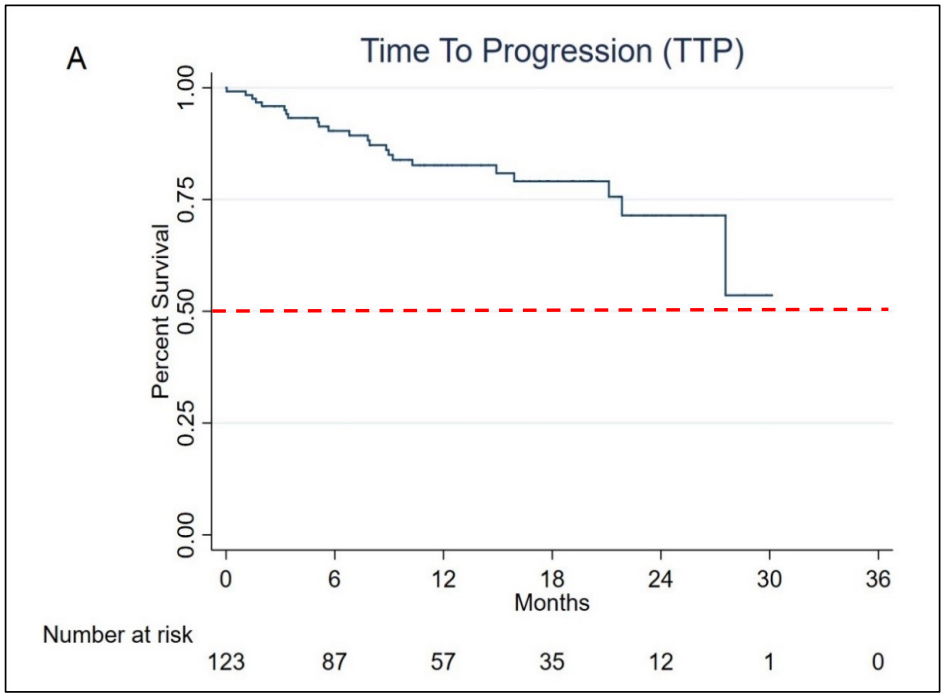


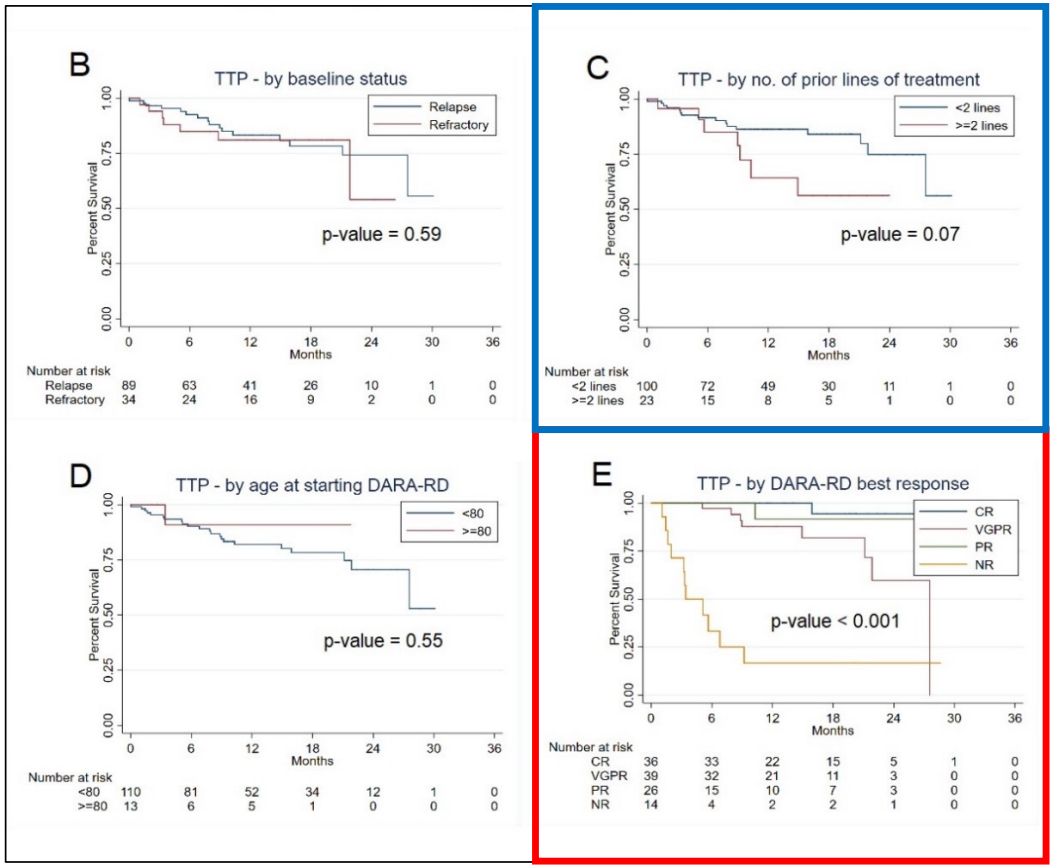




Median OS: NR; 1-years OS: 85.9%; 2-years OS: 73.7%

Nuove prospettive nel MIELOMA MULTIPLO

**Time to Progression** in a cohort of Multiple Myeloma patients treated with **DRd** (Panel A), and in subgroups of patients according to baseline status of relapse/refractory (Panel B), prior line of treatment (<2 vs >=2) (Panel C), age at starting DRd treatment (<80 vs ≥80) (Panel D) and best response to treatment (Panel E)

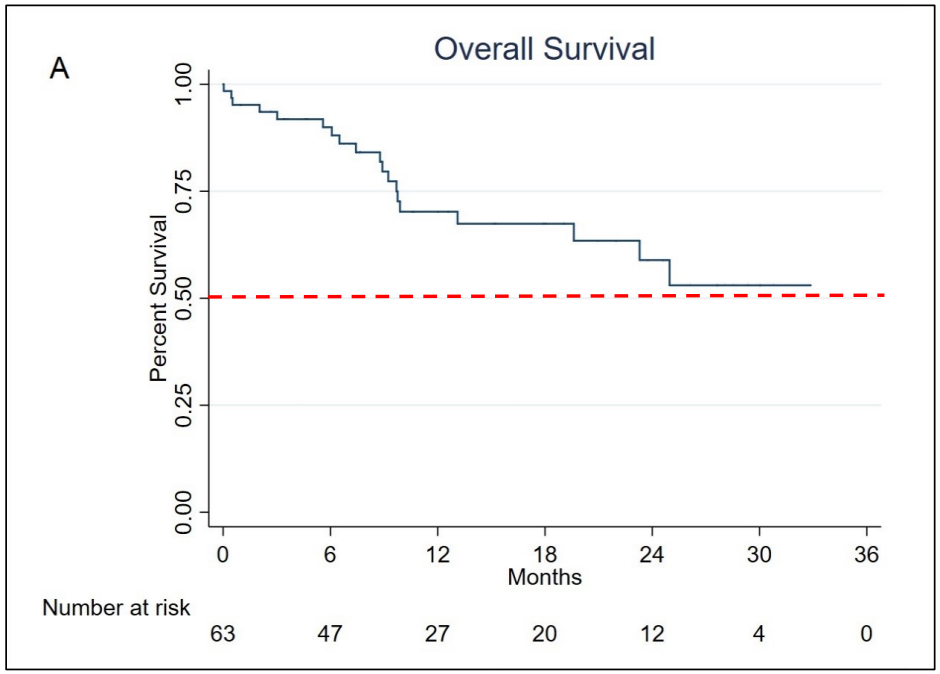


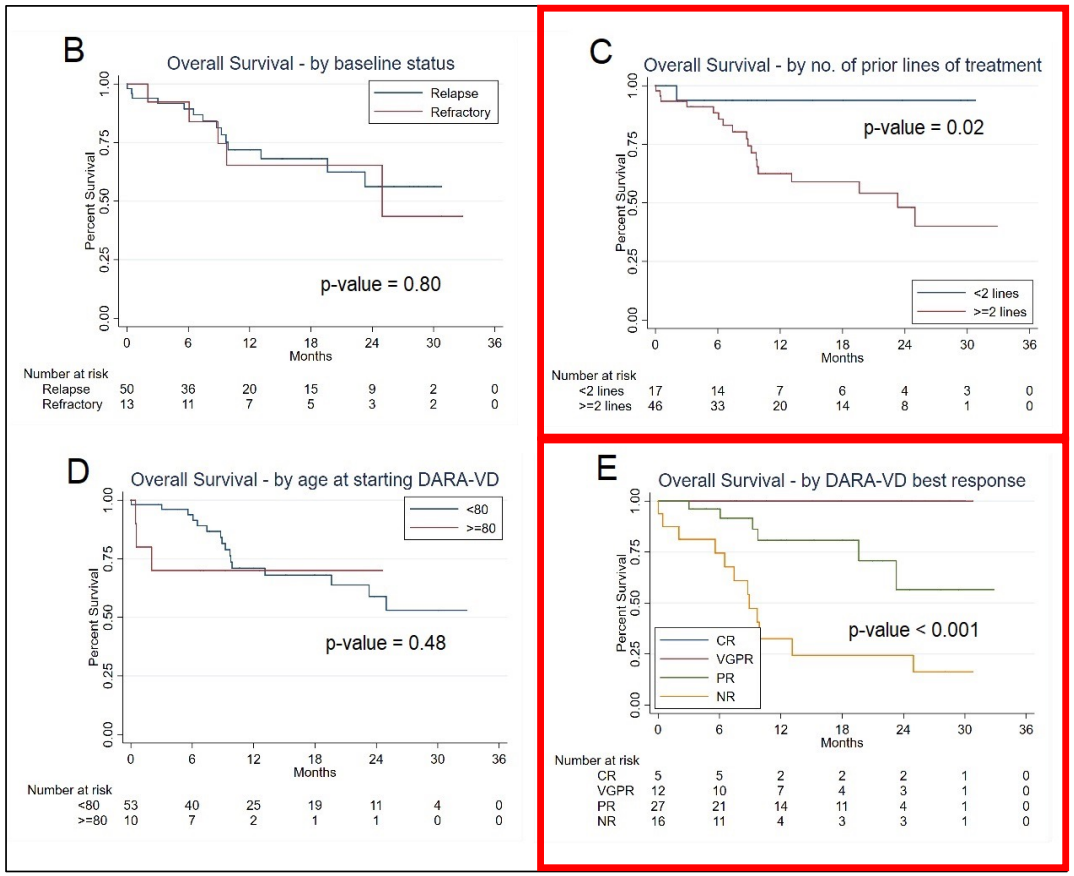




Median TTP: NR; 1-years TTP: 82.7%; 2-years TTP: 71.4%

Nuove prospettive nel MIELOMA MULTIPLO

**Overall Survival** in a cohort of multiple myeloma patients treated with **DVd** (Panel A), and in subgroups of patients according to baseline status of relapse/refractory (Panel B), prior line of treatment (<2 vs >=2) (Panel C), age at starting DVd treatment (<80 vs ≥80) (Panel D) and best response to treatment (Panel E)

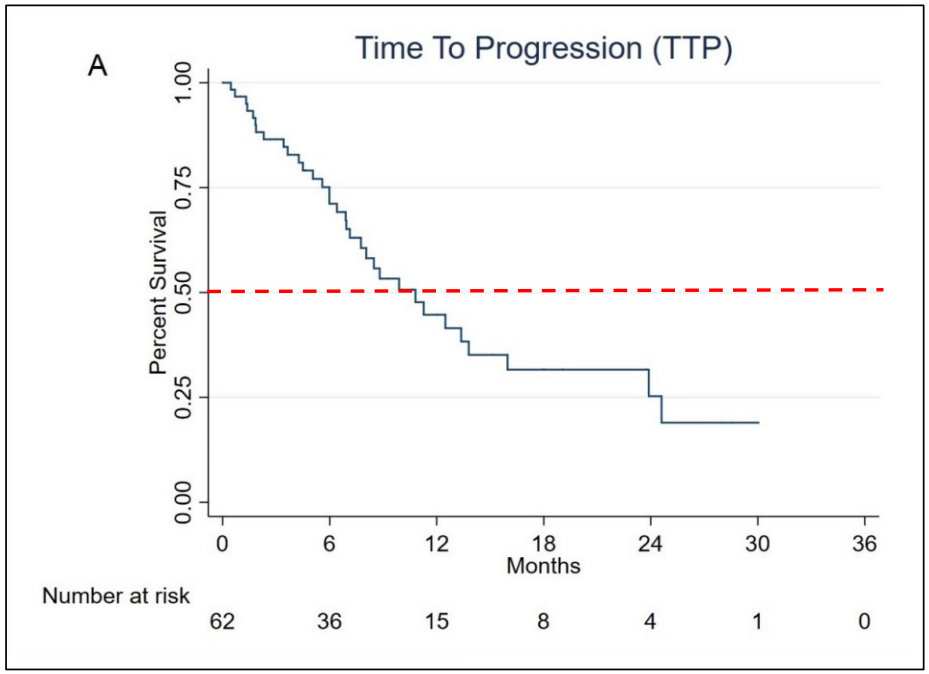


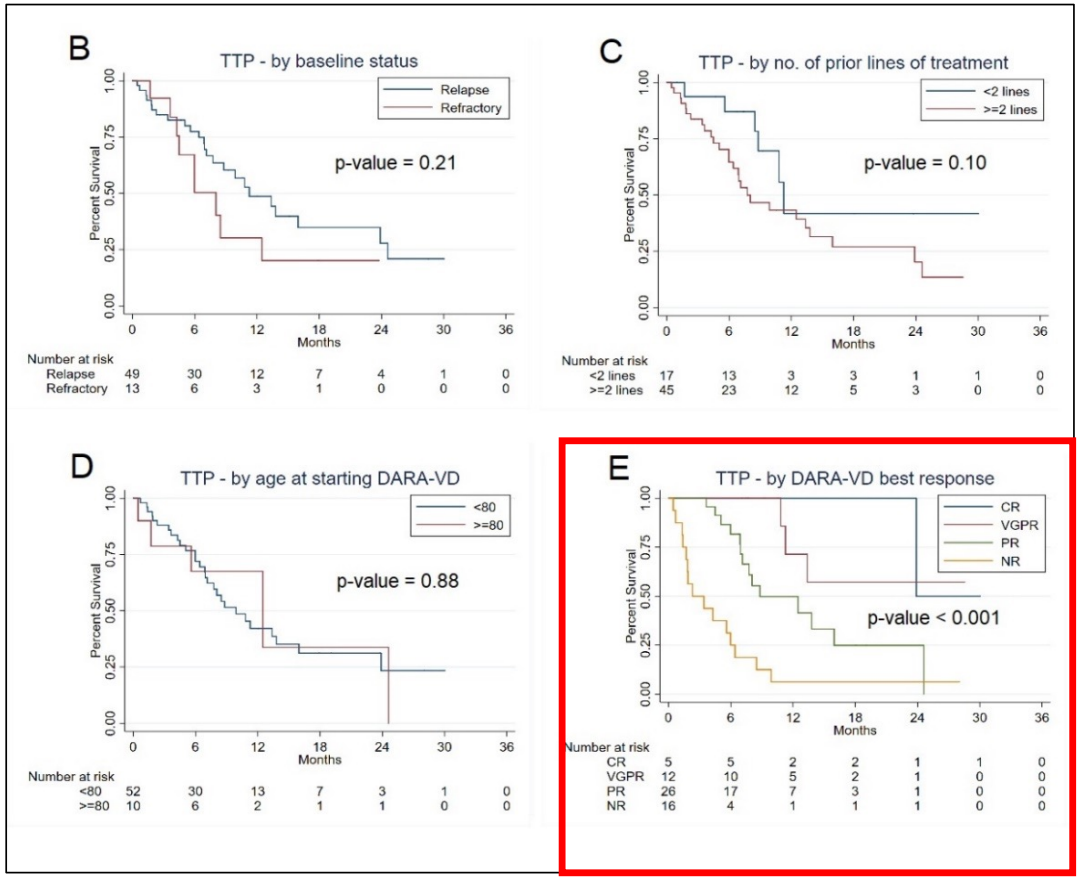




Median OS: NR; 1-years OS: 70.2%; 2-years OS: 58.9%

Nuove prospettive nel MIELOMA MULTIPLO

**Time to Progression** in a cohort of multiple myeloma patients treated with **DVd** (Panel A), and in subgroups of patients according to baseline status of relapse/refractory (Panel B), prior line of treatment (<2 vs >=2) (panel C), age at starting DVd treatment (<80 vs ≥80) (Panel D) and best response to treatment (Panel E)




Median TTP: 10,8 mesi (95%CI: 7.1-13.8); 1-years TTP: 44.7%; 2-years TTP: 25.3%

Nuove prospettive nel MIELOMA MULTIPLO

| | DARA-Vd | | | DARA-Rd | | | |
|---|---|---|---|---|---|---|---|
| | Studio Registrativo | Real-World | | | | | |
| | Studio Castor[1] | Esperienza REP | | | | | |
| **n. Pz** | **251** | **68** | | | | | |
| **mfollow-up** | **40,0 mesi** | **28 mesi** | | | | | |
| **Criteri di valutazione per la Risposta** | | | | | | | |
| **ORRs** | 85% | 74% | | | | | |
| **mTTR** | 1 mese | 1,5 mesi | | | | | |
| **mTTBR** | \\ | 4 mesi | | | | | |
| **mTTNT** | 9,7 mesi | \\ | | | | | |
| **mPFS/TTP** | PFS 16,7 mesi | TTP 10,8 mesi | | | | | |
| **mOS** | NR | NR | | | | | |
| **Tossicità (grado 3/4)** | | | | | | | |
| **Neutropenia** | 14% | 15,8% | | | | | |
| **PLTpenia** | 46% | 27,6% | | | | | |
| **Anemia** | 16% | 14% | | | | | |
| **Infezioni** | 13% | 17,2% | | | | | |


1. M.V. Mateos; Clinical Lymphoma, Myeloma & Leukemia 2020; 20(8):509-518
2. J.L. Kaufman; 61° ASH, Orlando, dicembre 7-10 2019
3. E. Antonioli et al.; L&L https://doi.org/10.1080/10428194.2020.1802452
4. F. Fazio et al.; eJHaem 2022; 1-8

| | DARA-Vd | | | DARA-Rd | | | |
|---|---|---|---|---|---|---|---|
| | Studio Registrativo | Real-World | | | | | |
| | Studio Castor[1] | Esperienza REP | Fazio F.[4] | | | | |
| **n. Pz** | **251** | **68** | **37** | | | | |
| **mfollow-up** | **40,0 mesi** | **28 mesi** | **13,49 mesi** | | | | |
| **Criteri di valutazione per la Risposta** | | | | | | | |
| **ORRs** | 85% | 74% | 72% | | | | |
| **mTTR** | 1 mese | 1,5 mesi | | | | | |
| **mTTBR** | \\ | 4 mesi | | | | | |
| **mTTNT** | 9,7 mesi | \\ | | | | | |
| **mPFS/TTP** | PFS 16,7 mesi | TTP 10,8 mesi | | | | | |
| **mOS** | NR | NR | | | | | |
| **Tossicità (grado 3/4)** | | | | | | | |
| **Neutropenia** | 14% | 15,8% | | | | | |
| **PLTpenia** | 46% | 27,6% | | | | | |
| **Anemia** | 16% | 14% | | | | | |
| **Infezioni** | 13% | 17,2% | | | | | |


1. M.V. Mateos; Clinical Lymphoma, Myeloma & Leukemia 2020; 20(8):509-518
2. J.L. Kaufman; 61° ASH, Orlando, dicembre 7-10 2019
3. E. Antonioli et al.; L&L https://doi.org/10.1080/10428194.2020.1802452
4. F. Fazio et al.; eJHaem 2022; 1-8

| | DARA-Vd | | | DARA-Rd | | | |
|---|---|---|---|---|---|---|---|
| | Studio Registrativo | Real-World | | Studio Registrativo | Real-World | | |
| | Studio Castor[1] | Esperienza REP | Fazio F.[4] | Studio Pollux[2] | Esperienza REP | | |
| **n. Pz** | **251** | **68** | **37** | **281** | **127** | | |
| **mfollow-up** | **40,0 mesi** | **28 mesi** | **13,49 mesi** | **54,9 mesi** | **28 mesi** | | |
| **Criteri di valutazione per la Risposta** | | | | | | | |
| **ORRs** | 85% | 74% | 72% | 93% | 85% | | |
| **mTTR** | 1 mese | 1,5 mesi | | 1 mese | 1 mese | | |
| **mTTBR** | \\ | 4 mesi | | \\ | 4,5 mesi | | |
| **mTTNT** | 9,7 mesi | \\ | | NR | \\ | | |
| **mPFS/TTP** | PFS 16,7 mesi | TTP 10,8 mesi | | PFS 45 mesi | TTP NR | | |
| **mOS** | NR | NR | | NR | NR | | |
| **Tossicità (grado 3/4)** | | | | | | | |
| **Neutropenia** | 14% | 15,8% | | 57% | 37,7% | | |
| **PLTpenia** | 46% | 27,6% | | 15% | 14,2% | | |
| **Anemia** | 16% | 14% | | 19% | 15,2% | | |
| **Infezioni** | 13% | 17,2% | | 18% | 17,3% | | |


1. M.V. Mateos; Clinical Lymphoma, Myeloma & Leukemia 2020; 20(8):509-518
2. J.L. Kaufman; 61° ASH, Orlando, dicembre 7-10 2019
3. E. Antonioli et al.; L&L https://doi.org/10.1080/10428194.2020.1802452
4. F. Fazio et al.; eJHaem 2022; 1-8

| | DARA-Vd | | | DARA-Rd | | | |
|---|---|---|---|---|---|---|---|
| | Studio Registrativo | Real-World | | Studio Registrativo | Real-World | | |
| | Studio Castor[1] | Esperienza REP | Fazio F.[4] | Studio Pollux[2] | Esperienza REP | Antonioli E.[3] | |
| **n. Pz** | **251** | **68** | **37** | **281** | **127** | **44** | |
| **mfollow-up** | **40,0 mesi** | **28 mesi** | **13,49 mesi** | **54,9 mesi** | **28 mesi** | **8 mesi** | |
| **Criteri di valutazione per la Risposta** | | | | | | | |
| **ORRs** | 85% | 74% | 72% | 93% | 85% | 79% | |
| **mTTR** | 1 mese | 1,5 mesi | | 1 mese | 1 mese | 45 giorni | |
| **mTTBR** | \\ | 4 mesi | | \\ | 4,5 mesi | \\ | |
| **mTTNT** | 9,7 mesi | \\ | | NR | \\ | \\ | |
| **mPFS/TTP** | PFS 16,7 mesi | TTP 10,8 mesi | | PFS 45 mesi | TTP NR | NR | |
| **mOS** | NR | NR | | NR | NR | NR | |
| **Tossicità (grado 3/4)** | | | | | | | |
| **Neutropenia** | 14% | 15,8% | | 57% | 37,7% | 56% | |
| **PLTpenia** | 46% | 27,6% | | 15% | 14,2% | 9% | |
| **Anemia** | 16% | 14% | | 19% | 15,2% | 7% | |
| **Infezioni** | 13% | 17,2% | | 18% | 17,3% | 32% | |


1. M.V. Mateos; Clinical Lymphoma, Myeloma & Leukemia 2020; 20(8):509-518
2. J.L. Kaufman; 61° ASH, Orlando, dicembre 7-10 2019
3. E. Antonioli et al.; L&L https://doi.org/10.1080/10428194.2020.1802452
4. F. Fazio et al.; eJHaem 2022; 1-8

| | DARA-Vd | | | DARA-Rd | | | |
|---|---|---|---|---|---|---|---|
| | Studio Registrativo | Real-World | | Studio Registrativo | Real-World | | |
| | Studio Castor[1] | Esperienza REP | Fazio F.[4] | Studio Pollux[2] | Esperienza REP | Antonioli E.[3] | Fazio F.[4] |
| **n. Pz** | **251** | **68** | **37** | **281** | **127** | **44** | **126** |
| **mfollow-up** | **40,0 mesi** | **28 mesi** | **13,49 mesi** | **54,9 mesi** | **28 mesi** | **8 mesi** | **13,49 mesi** |
| **Criteri di valutazione per la Risposta** | | | | | | | |
| **ORRs** | 85% | 74% | 72% | 93% | 85% | 79% | 87% |
| **mTTR** | 1 mese | 1,5 mesi | | 1 mese | 1 mese | 45 giorni | |
| **mTTBR** | \\ | 4 mesi | | \\ | 4,5 mesi | \\ | |
| **mTTNT** | 9,7 mesi | \\ | | NR | \\ | \\ | |
| **mPFS/TTP** | PFS 16,7 mesi | TTP 10,8 mesi | | PFS 45 mesi | TTP NR | NR | |
| **mOS** | NR | NR | | NR | NR | NR | |
| **Tossicità (grado 3/4)** | | | | | | | |
| **Neutropenia** | 14% | 15,8% | | 56% | 37,7% | 56% | |
| **PLTpenia** | 46% | 27,6% | | 15% | 14,2% | 9% | |
| **Anemia** | 16% | 14% | | 18% | 15,2% | 7% | |
| **Infezioni** | 13% | 17,2% | | 16% | 17,3% | 32% | |


1. M.V. Mateos; Clinical Lymphoma, Myeloma & Leukemia 2020; 20(8):509-518
2. J.L. Kaufman; 61° ASH, Orlando, dicembre 7-10 2019
3. E. Antonioli et al.; L&L https://doi.org/10.1080/10428194.2020.1802452
4. F. Fazio et al.; eJHaem 2022; 1-8

## TAKE MESSAGES

- dati di efficacia e tossicità sostanzialmente sovrapponibili ai dati riportati dagli studi registrativi (nel gruppo DARA-Rd, TTP e OS non raggiunte, nel gruppo DARA-Vd OS non raggiunta, TTP 10.8 mesi)
- L' " *età ≥80 aa*«, a nostro avviso, non rappresenta una controindicazione assoluta all'impiego delle triplette DARA-based
- Il valore della " *Clearence della Creatinina*", a nostro avviso, non rappresenta una contraindicazione assoluta all'impiego della tripletta DARA-Rd
- Efficacia della tripletta DARA-Rd anche nei pazienti "*Lena-Refractory*", sebbene il n. dei pazienti sia molto piccolo