

News dal mondo “LINFOMI”



NAPOLI - 18 SETTEMBRE 2023 - ROYAL HOTEL CONTINENTAL

RUOLO DEL PEMBROLIZUMAB COME BRIDGE ALL'AUTOTRAPIANTO

GIULIANA FARINA
AORN S.ANNA E SAN SEBASTIANO
CASERTA

DONNA 41 ANNI

01.06.2021 = Dgn di NHL PMBCL da mediastinica eseguita il 25.05.2021 (c/o Chirurgia Toracica AO dei Colli – Monaldi)

Sintomi: sdr mediastinica da compressione della cava e trombosi giugulare int dx/v brachio-cefalica dx estesa fino alla confluenza della VCS

Comorbidità:

Trombofilia, eterozigote MTHFR e omozigote PAI.

ADR polvere, pollini, acari, parietaria.

Stadiazione

PET (03.05.2021) = captazione mediastino ant sup SUV 8,9; captazione a livello dell'utero (SUV 4,1) compatibile con *captazione aspecifica*.

BOM (esordio) neg

1° linea

DA-R/EPOCH x n 6 cicli + 2 Rituximab
(06.2021 -> 15.12.2021)

Restaging interm post IV ciclo

PET 09.09.2021, = captazione mediastino ant sup (SUV 2,2)

Restaging finale post VI ciclo

PET 03.01.2022, captazione mediastino ant sup (SUV 7,5) in sede tracheale/paratracheale sup dx (SUV 8,6) livello reg iliaca sx (SUV 9,2).

Paz “primary refractory”.

TORRESE BENEDETTA (41y) - 03/05/2021 11:56:29 - TC FUSIONE

Im: 118/319
Se: 3

A

T

L



You have 12 days left in your trial period.
Purchase a license at <https://radiantviewer.com/store/>
This session will end in 1 minute.

WL: 40 WW: 400 [D]
T: 3.8mm L: -329.5mm

56mA 120kV
03/05/2021 11:56:29

TORRESE BENEDETTA (41y) - 09/09/2021 10:55:55 - TC FUSIONE

Im: 120/319
Se: 3

A

TO

L



You have 12 days left in your trial period.
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This session will end in 1 minute.

WL: 40 WW: 400 [D]
T: 3.8mm L: -335.1mm

126mA 120kV
09/09/2021 10:55:55

TORRESE BENEDETTA (41y) - 03/05/2021 12:04:21 - WB FX

Im: 118/319
Se: 12

A

L



You have 12 days left in your trial period.
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This session will end in 1 minute.

X: 37 Y: 66 Val: 1.973
Max: 74659 (25%) [D] N
T: 2.8mm L: -329.5mm

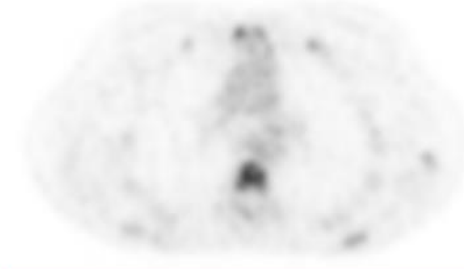
03/05/2021 12:02:18

TORRESE BENEDETTA (41y) - 09/09/2021 11:03:58 - WB FX

Im: 120/319
Se: 12

A

L



You have 12 days left in your trial period.
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This session will end in 1 minute.

Max: 25651 (25%) [D] N
T: 2.8mm L: -335.1mm

09/09/2021 11:01:55

Febbraio 2022: biopsia linf ECO-guidata reg iliaca sx

DESCRIZIONE MICROSCOPICA

Il presente campione è costituito da un frustolo bioptico sede di proliferazione mesenchimale a cellule con chiari caratteri morfologici di malignità. Marginalmente si osservano due piccole aree di infiltrazione linfoide (LCA +), nelle quali sono presenti elementi di grossa taglia, con nuclei ipercromatici ed iperplasi, positivi alle colorazioni immunohistochimiche per CD79a, bcl-6 e MUM-1 e negative a quelle per CD10, con focale espressione di CD23. L'indice di proliferazione cellulare Ki-67 appare elevato (circa 60%) in quella linfoide ed irrilevante in quella mesenchimale.

RDHAP x 2



PET 21.04.2022: persistenza di malattia



Quale scelta terapeutica è più opportuna

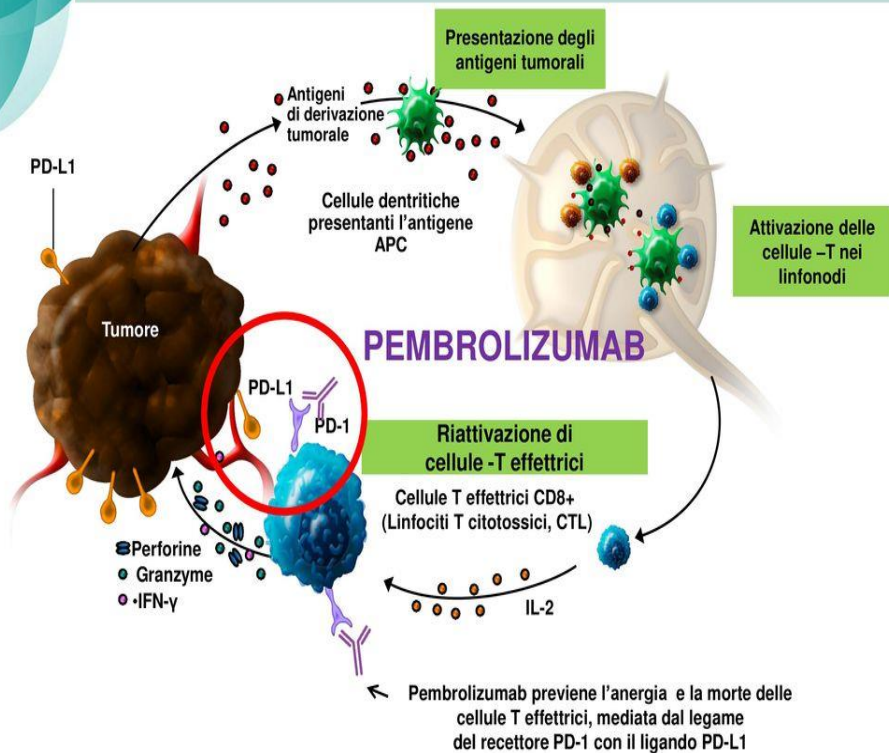
AUTOBMT?

CAR-T?

TANDEM AUTO –ALLO O CAR-T

BRIDGE THERAPY?

Pembrolizumab: Meccanismo di Azione



Frequent amplification and translocation events occur at 9p24.1 in PMBCL, resulting in tumor expression of the programmed cell death-1 (PD-1) ligands PD-L1 and PD-L2.11-14 This suggests susceptibility of PMBCL to PD-1 blockade.

KEYNOTE-170/KEYNOTE-013 Pembrolizumab in R/R PMBCL: Background

- R/R PMBCL associated with poor outcomes, few treatment options^[1]
- Genetic abnormalities (eg, activation of NF- κ B, JAK/STAT^[2]; amplification/translocation of 9p24^[3-6]) often lead to overexpression of PD-L1 and PD-L2 in PMBCL
 - May be sensitive to PD-1 blockade
- Pembrolizumab: humanized IgG4 monoclonal antibody against PD-1
- Phase Ib KEYNOTE-013 showed preliminary efficacy, safety of pembrolizumab in PMBCL^[1]
 - 41% ORR; 12% CR rate; median DoR not reached
- Phase II KEYNOTE-170 extends KEYNOTE-013 and adds biomarker analyses^[1]
- Current analysis presents updated safety, efficacy data from KEYNOTE-013 and full KEYNOTE-170 cohort with pembrolizumab in patients with R/R PMBCL

1. Armand. ASH 2018. Abstr 228. 2. Savage. Blood. 2003;12:3871. 3. Green. Blood. 2010;17:3266.
4. Twa. Blood. 2014;123:2062. 5. Shi. Am J Surg Path. 2014;38:1715. 6. Chen. Clin Can Res. 2013;13:3462.



Slide credit: clinicaloptions.com

KEYNOTE-170/KEYNOTE-013 Pembrolizumab in R/R PMBCL: Study Design

Phase Ib KEYNOTE-013

R/R PMBCL patients
≥ 18 yrs of age without
ASCT*
(N = 21)



Pembrolizumab
10 mg/kg Q2W (patients 1-10)
or 200 mg Q3W (patients 11-21)



*Treatment up to 2 yrs or
until unacceptable toxicity,
PD, or study withdrawal*

Response assessment by PET/CT scan:

- KEYNOTE-013: Wk 12 then Q8W (10 mg/kg Q2W) or Wks 6, 12 then Q9W (200 mg Q3W), IWG 2007 criteria
- KEYNOTE-170: Wk 12 then Q12W, IWG 2007 criteria

Phase II KEYNOTE-170

R/R PMBCL patients
≥ 18 yrs of age without
ASCT,* failed ≥ 2
prior regimens
(N = 53)



Pembrolizumab
200 mg Q3W



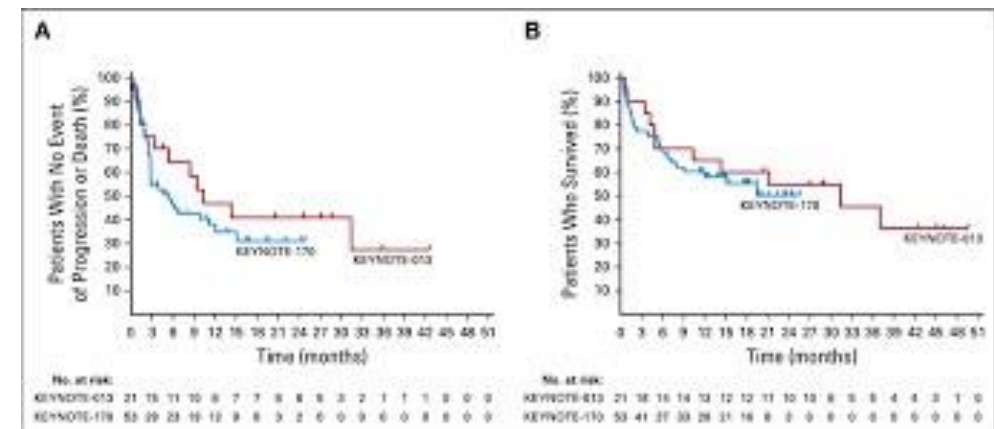
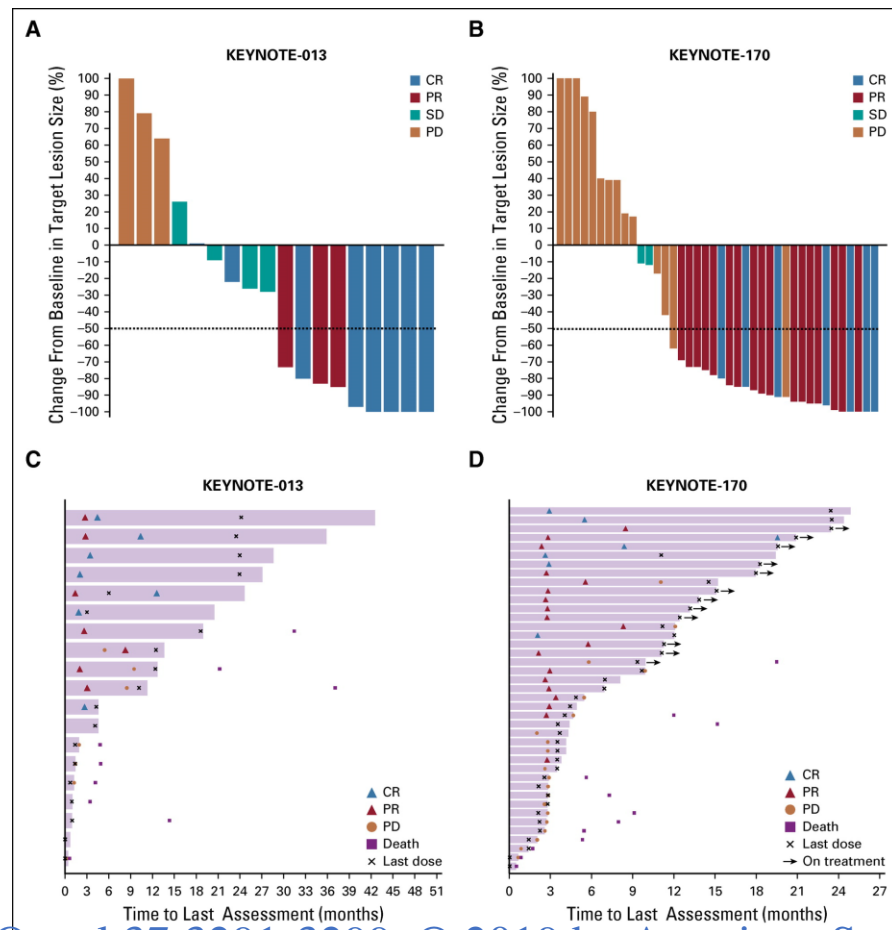
*Treatment up to 2 yrs or
until unacceptable toxicity,
PD, or study withdrawal*

Primary endpoints: ORR, safety (KEYNOTE-013 only)

Secondary endpoints: DoR, PFS, OS, safety (KEYNOTE-170)

*Failed, ineligible, or refused.





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MAGGIO 2022

Pembrolizumab ogni 2 settimane off label : 4 dosi totali

GIUGNO 2022

PET : mediastino (SUV 13,5 vs 7,5).

Quadro suggestivo per PD (Deauville score = 5).

sospetto di **“tumor flare”**

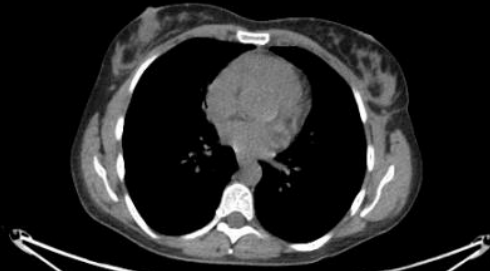
netto miglioramento clinico riferito dalla paz

TC Torace mdc del 28.06.2022 (post n 4 Pembro) = Riduzione volumetrica del noto tessuto solido ipodenso (28x25 mm vs 79x63 mm) a carico del mediastino ant-sup.

TORRESE BENEDETTA (41y) - 22/03/2022 14:58:53 - CT FUSIONE

Im: 106/351
Se: 3

R



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WL: 40 WW: 400 [D]
T: 3.8mm L: -330.0mm

P

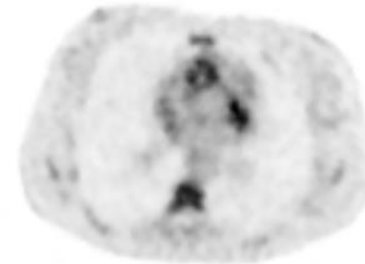
32mA 120kV
22/03/2022 14:58:53

L

TORRESE BENEDETTA (41y) - 22/03/2022 15:06:31 - PET QC

Im: 103/345
Se: 12

R



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Max: 9807 (25%) [D] N
T: 2.8mm L: -328.8mm

P

22/03/2022 15:04:59

ANTERIORE

TORRESE BENEDETTA (42y) - 23/06/2022 15:00:31 - CT FUSIONE

Im: 97/280
Se: 3

R



You have 12 days left in your trial period.
Purchase a license at <https://radiantviewer.com/store/>

WL: 40 WW: 400 [D]
T: 3.8mm L: -430.4mm

P

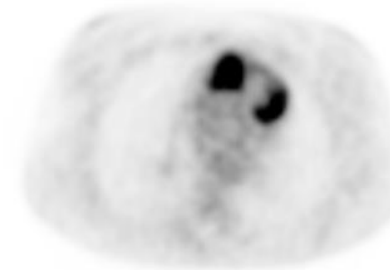
53mA 120kV
23/06/2022 15:00:31

L

TORRESE BENEDETTA (42y) - 23/06/2022 15:14:24 - WB 3IT

Im: 88/263
Se: 6

R



You have 12 days left in your trial period.
Purchase a license at <https://radiantviewer.com/store/>

Max: 16628 (5%) N
T: 3.3mm L: -430.0mm

P

23/06/2022 15:10:21

L

TORRESE BENEDETTA (41y) - 22/03/2022 14:58:53 - CT FUSIONE

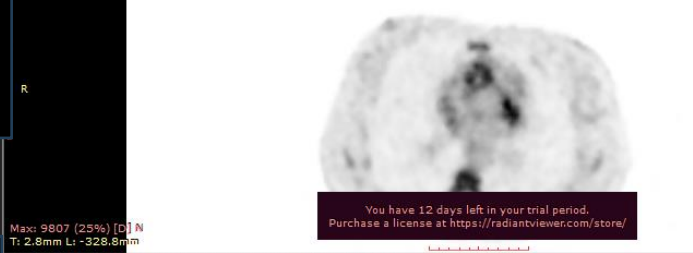
Im: 106/351
Se: 3



32mA 120kV

TORRESE BENEDETTA (41y) - 22/03/2022 15:04:59 - PET QC

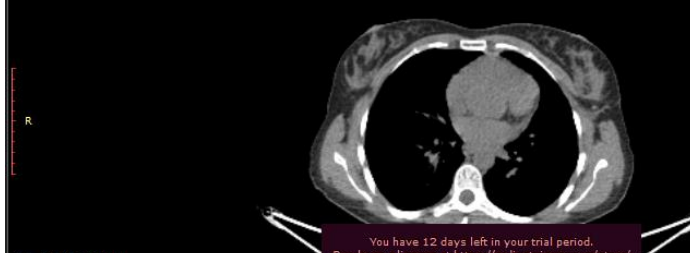
Im: 103/345
Se: 12



22/03/2022 15:04:59

TORRESE BENEDETTA (42y) - 23/06/2022 15:00:31 - CT FUSIONE

Im: 97/280
Se: 3



53mA 120kV

TORRESE BENEDETTA (42y) - 23/06/2022 15:10:21 - WB 3IT

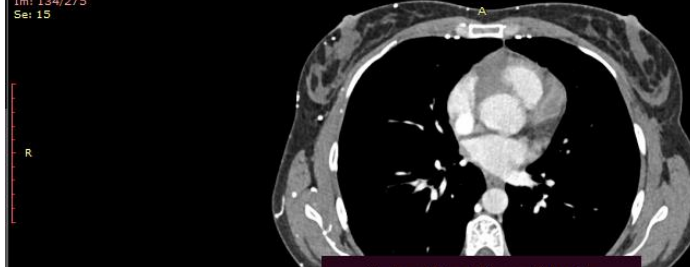
Im: 88/263
Se: 6



23/06/2022 15:10:21

TORRESE BENEDETTA (42y) - 28/06/2022 16:08:32 - Venosa 1,50 Br40 S3 ax Mediastino

Im: 134/275
Se: 15



26mA 130kV

28/06/2022 16:08:27

Agosto 2022

consolidamento terapeutico con **ASCT** previa HDT sec schema
FEAM.

Rivalutazione PET TAC dopo trapianto : CR



Follow up
Mantenimento

Novembre 2022 —→ APRILE 2023
mantenimento per 12 somministrazioni

Ultimo follow up luglio 2023 PET TAC : CR

CONCLUSIONI

LA LETTERATURA SUPPORTA L'EFFICACIA DI KEYTRUDA E LA DURATA DELLA RISPOSTA IN PMBCL R/R

IL PROFILO DI TOSSICITÀ È ESTREMAMENTE MANEGGEVOLE

I PZ CHE NON IPERESPRESIMONO PD1L/2L HANNO UNA PROGNOSI PEGGIORE

QUALE SIA 'ESAME STRUMENTALE PIÙ UTILE NEL RESTAGING TAC e/o PET E ' DA CHIARIRE E PONE MOLTI INTERROGATIVI

PER EFFICACIA DI UNA TERAPIA DI MANTENIMENTO SERVONO STUDI FUTURI

grazie