LINFOMA DI HODGKIN E LINFOMI NON HODGKIN A BASSO GRADO DI AGGRESSIVITÀ

CONTRIBUTI DELL'EMATOLOGIA BOLOGNESE

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Disclosures

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other

[Splenectomy in the therapy of Hodgkin's lymphoma]

[Article in Italian]

S Tura, F Lauria, M Baccarani

Haematologica. 1972;57(9):465-80.

[Use of total radiotherapy in Hodgkin's lymphoma]

[Article in Italian]

L Babini, C Rimondi, C Putti, R Sciascia, B Teofoli, F Lauria, M Baccarani, S Tura

Haematologica. 1972;57(9):481-7.

LINFOMA DI HODGKIN

Letters to the Editor

COMBINATION CHEMOTHERAPY IN STAGES I OR II HODGKIN'S DISEASE

Francesco Lauria, Michele Baccarani, Mauro Fiacchini, Patrizio Mazza, Sante Tura

Lancet. 1979 Nov 17;2(8151):1072-3.

Management of nodular sclerosis Hodgkin's disease stage I, II A and B: evidence for a beneficial effect of MOPP on the relapse rate

F Lauria, M Baccarani, L Babini, E Emiliani, M Fiacchini, M Gobbi, P Mazza, R Sciascia, S Tura

Acta Haematol. 1979;62(5-6):262-6.

Haematologica. 1979 Feb;64(1):50-60.

The effect of chemotherapy (MOPP) following radiotherapy in stage I to III Hodgkin's disease: analysis of 110 cases

S Tura, F Lauria, M Baccarani, M Fiacchini, R Frezza, P Mazza, L Babini, R Sciascia, E Emiliani, E Barbieri

Eur J Cancer Clin Oncol. 1984 Nov;20(11):1393-9.

Prognostic significance of lymphography in stage IIIs Hodgkin's disease (HD)

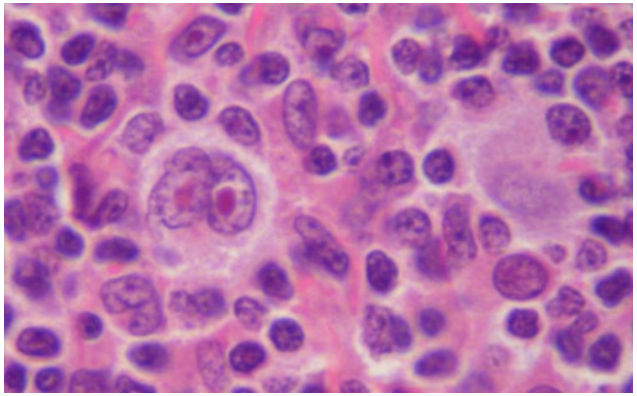
P Mazza, G Miniaci, F Lauria, M Gobbi, E Emiliani, E Barbieri, S Neri, P Querzani, M Fiacchini, S Tura

LINFOMA DI HODGKIN

Eur J Cancer Clin Oncol. 1986 Nov;22(11):1315-23.

Hodgkin's disease (HD): a historical perspective

S Tura, P Mazza, P L Zinzani, F Verlicchi, M Baccarani, F Lauria, M Fiacchini, M Gobbi, G Bandini, E Emiliani, et al.



507 patients with HL, forming the basis of our 18 years experience, retrospectively analyzed

Four therapeutic periods are recognizable:

- **The 1966-1970 period was characterized by the absence of treatment and management policy**
- **The 1971-1974 period was characterized by the increasing knowledge of staging relevance and therapeutic approaches**
- **The 1975-1980 period was characterized by a large combination of MOPP and radiotherapy**
- **The last therapeutic period (1980 to present time) is characterized by the increasing relevance of prognostic factors and alternating use of MOPP and ABVD**

The 83 patients who entered this period showed 90% survival at 5 yr

The ABVD ERA

LINFOMA DI HODGKIN BV

haematologica | 2013; 98(8)

Brentuximab vedotin in relapsed/refractory Hodgkin's lymphoma: the Italian experience and results of its use in daily clinical practice outside clinical trials

Pier Luigi Zinzani,[1] Simonetta Viviani,[2] Antonella Anastasia,[3] Umberto Vitolo,[4] Stefano Luminari,[5] Francesco Zaja,[6] Paolo Corradini,[7] Michele Spina,[8] Ercole Brusamolino,[9] Alessandro M. Gianni,[2] Armando Santoro,[3] Barbara Botto,[4] Enrico Derenzini,[1] Cinzia Pellegrini,[1] and Lisa Argnani[1]

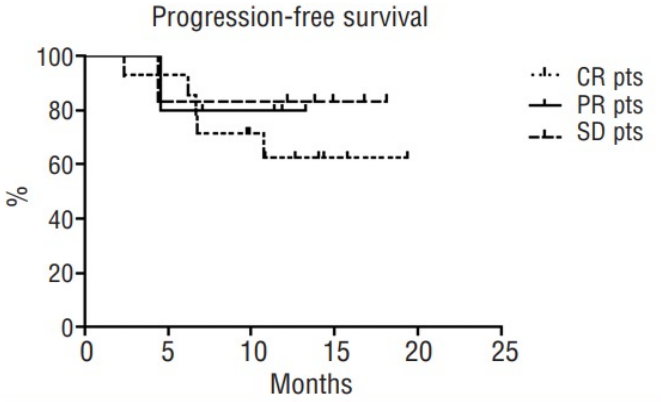


Figure 4. Progression-free survival of patients divided according to response. CR: complete response; PR: partial response; SD: stable disease; pts, patients.

- These data on BV in patients treated within the NPP indicate that this drug is highly effective and very well tolerated also in standard everyday clinical practice, i.e. outside the clinical trial setting, in relapsed/refractory HL.
- With regards to toxicity, peripheral neuropathy was the most common side effect, although it was less frequent than in the pivotal phase II study.
- In terms of effectiveness, this report confirms the trend of complete response and overall response rates

LINFOMA DI HODGKIN BV

haematologica 2020; 105:e512

Vittorio Stefoni,[1] Miriam Marangon,[1*] Alessandro Re,[2] Arben Lleshi,[3] Maurizio Bonfichi,[4] Antonello Pinto,[5] Nicola Bianchetti,[2] Cinzia Pellegrini,[4] Lisa Argnani[1] and Pier Luigi Zinzani[1]*

Brentuximab vedotin in the treatment of elderly Hodgkin lymphoma patients at first relapse or with primary refractory disease: a phase II study of FIL ONLUS

With a median follow-up of 24.9 months, median PFS was 8.8 months and median OS was 21.7 months. 1-year PFS and OS were 40% and68.8%, respectively (Figure 1-2).

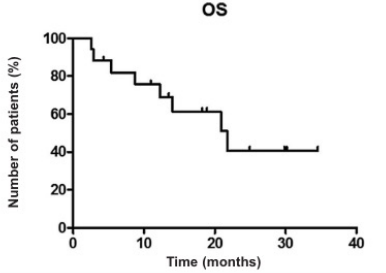


Figure 1. Patients' overall survival (OS).

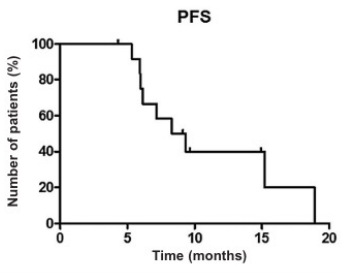


Figure 2. Patients' progression free survival (PFS).

The Oncologist 2015;20:1413–1416

Brentuximab Vedotin in Transplant-Naïve Relapsed/Refractory Hodgkin Lymphoma: Experience in 30 Patients

Pier Luigi Zinzani,[a] Cinzia Pellegrini,[a] Maria Cantonetti,[b] Alessandro Re,[c] Antonello Pinto,[d] Vincenzo Pavone,[e] Luigi Rigacci,[f] Melania Celli,[a] Alessandro Broccoli,[a] Lisa Argnani,[a] Alessandro Pulsoni[g]

30 pts with relapsed/refractory HL- and PET-positive disease after conventional chemotherapy salvage treatments were treated with a median of 4 cycles of BV. Normalization of PET findings (Deauville score ≤2) occurred in 9 of 30 patients (30%). Those nine patients proceeded to ASCT.

LINFOMA DI HODGKIN BV

Oncotarget, 2017, Vol. 8, (No. 53),

Italian real life experience with brentuximab vedotin: results of a large observational study on 234 relapsed/refractory Hodgkin's lymphoma

Cinzia Pellegrini[1,*], Alessandro Broccoli[1,*], Alessandro Pulsoni[2], Luigi Rigacci[3], Caterina Patti[4], Guido Gini[5], Donato Mannina[6], Monica Tani[7], Chiara Rusconi[8], Alessandra Romano[9], Anna Vanazzi[10], Barbara Botto[11], Armando Santoro[12], Stefan Hoaus[13], Gian Matteo Rigolin[14], Pellegrino Musto[15], Patrizio Mazza[16], Stefano Molica[17], Paolo Corradini[18], Angelo Fama[19], Francesco Gaudio[20], Michele Merli[21], Fioravante Ronconi[22], Giuseppe Gritti[23], Daniele Vallisa[24], Patrizia Tosi[25], Anna Marina Liberati[26], Antonello Pinto[27], Vincenzo Pavone[28], Filippo Gherlinzoni[29], Maria Paola Bianchi[30], Stefano Volpetti[31], Livio Trentin[32], Maria Cecilia Goldaniga[33], Maurizio Bonfichi[34], Amalia De Renzo[35], Corrado Schiavotto[36], Michele Spina[37], Angelo Michele Carella[38], Vittorio Stefoni[1], Lisa Argnani[1] and Pier Luigi Zinzani[1]

The results of this large retrospective study on 234 R/R HL in the real world support the effectiveness of BV with a manageable toxicity as previously reported also in clinical trials; in particular, our report confirms activity also in elderly patients, duration of the clinical response unrelated to the consolidation with transplant procedure, the relevance of the CR status at first restaging for the quality of the final response, and the role of BV as a bridge to ASCT for chemorefractory patients.

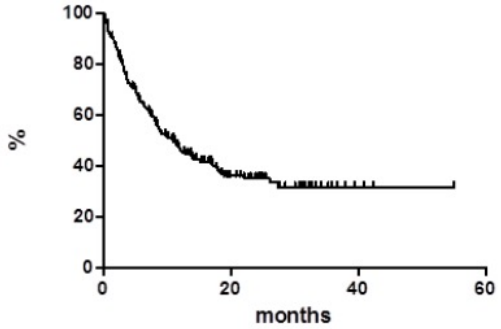


Figure 2: Progression free survival.

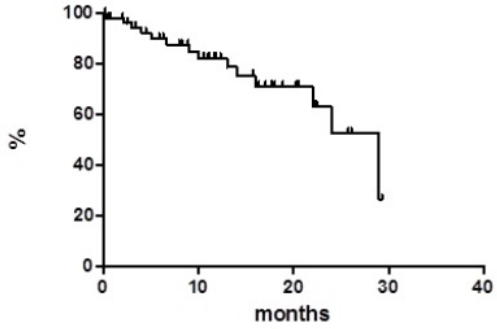


Figure 3: Disease free survival.

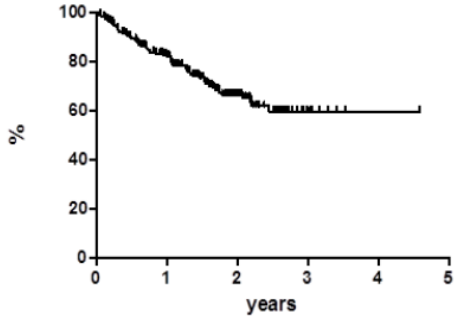


Figure 1: Overall survival.

LINFOMA DI HODGKIN BV AVD

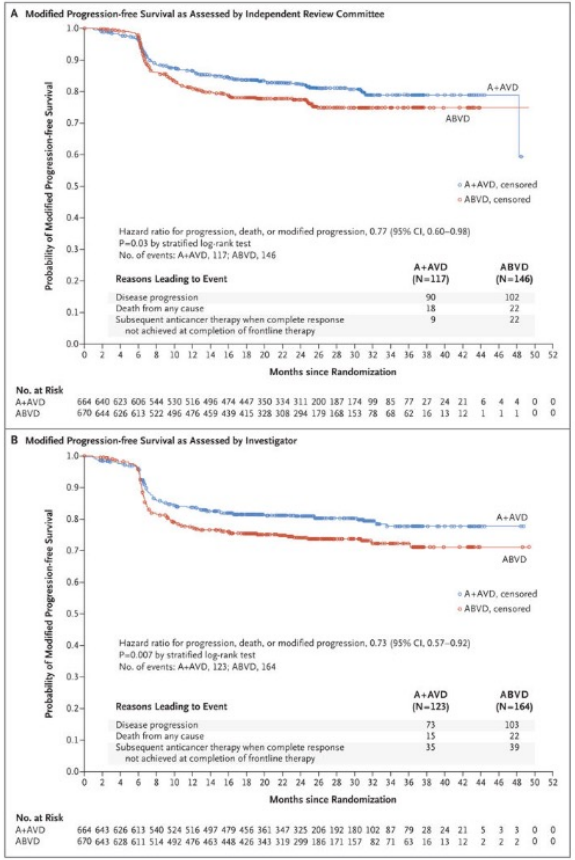
N Engl J Med. 2018 January 25; 378(4):

Brentuximab Vedotin with Chemotherapy for Stage III or IV Hodgkin's Lymphoma

J.M. Connors, W. Jurczak, D.J. Straus, S.M. Ansell, W.S. Kim, A. Gallamini, A. Younes, S. Alekseev, Á. Illés, M. Picardi, E. Lech-Maranda, Y. Oki, T. Feldman, P. Smolewski, K.J. Savage, N.L. Bartlett, J. Walewski, R. Chen, R. Ramchandren, P.L. Zinzani, D. Cunningham, A. Rosta, N.C. Josephson, E. Song, J. Sachs, R. Liu, H.A. Jolin, D. Huebner, J. Radford, and for the ECHELON-1 Study Group*

ECHELON-1

Brentuximab vedotin plus AVD, as compared with standard treatment with ABVD, resulted in a statistically significant and clinically meaningful improvement in the rate of modified progression-free survival



LINFOMA DI HODGKIN anti PD 1

Lancet Oncol 2021; 22: 512–24

Pembrolizumab versus brentuximab vedotin in relapsed or refractory classical Hodgkin lymphoma (KEYNOTE-204): an interim analysis of a multicentre, randomised, open-label, phase 3 study

*John Kuruvilla, Radhakrishnan Ramchandren, Armando Santoro, Ewa Paszkiewicz-Kozik, Robin Gasiorowski, Nathalie A Johnson, Laura Maria Fogliatto, Iara Goncalves, Jose S R de Oliveira, Valeria Buccheri, Guilherme F Perini, Neta Goldschmidt, Iryna Kriachok, Michael Dickinson, Mieczyslaw Komarnicki, Andrew McDonald, Muhit Ozcan, Naohiro Sekiguchi, Ying Zhu, Akash Nahar, Patricia Marinello, Pier Luigi Zinzani, on behalf of the KEYNOTE-204 investigators**

In conclusion, results from the KEYNOTE-204 study suggest that pembrolizumab should be considered the preferred treatment option for patients with relapsed or refractory classical Hodgkin lymphoma who have relapsed after autologous HSCT or are ineligible for autologous HSCT.

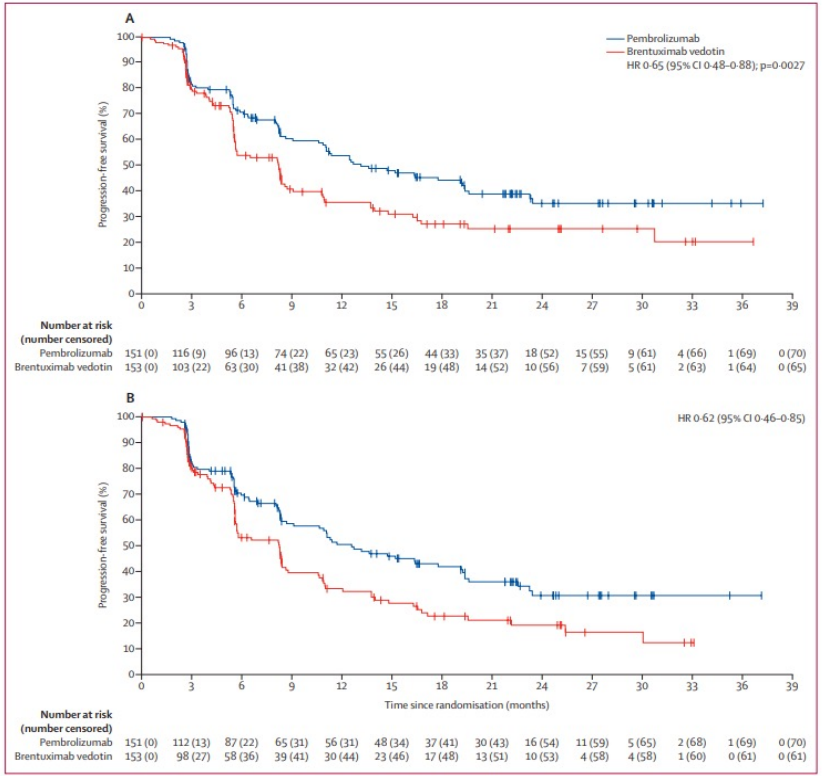


Figure 2: **Progression-free survival by blinded independent central review per International Working Group 2007 criteria**
Progression-free survival including (A) or excluding (B) clinical and imaging data following autologous HSCT or allogeneic HSCT. HSCT=haematopoietic stem-cell transplantation. HR=hazard ratio. HRs based on Cox regression model with Efron's method of tie-handling, with treatment as a covariate stratified by previous autologous HSCT (yes *vs* no) and classical Hodgkin lymphoma status after front-line therapy (primary refractory *vs* relapsed <12 months after completion of front-line therapy *vs* relapsed ≥12 months after completion of front-line therapy). One-sided p value based on log-rank test stratified by the same parameters as the HR.

LINFOMA DI HODGKIN anti PD 1

Cancer Medicine. 2020;9:7830–7836.

Effectiveness of chemotherapy after anti-PD-1 blockade failure for relapsed and refractory Hodgkin lymphoma

Beatrice Casadei | Lisa Argnani | Alice Morigi | Ginevra Lolli | Alessandro Broccoli | Cinzia Pellegrini | Laura Nanni | Vittorio Stefoni | Paolo E. Coppola | Matteo Carella | Michele Cavo | Pier Luigi Zinzani

Our results are in line with what previously observed, supporting the hypothesis of a **new chemo-sensitization** due to anti-PD1 treatment in HL patients with highly pre-treated and chemo-refractory disease. This approach gave also a chance for some patients to receive consolidation with SCT (both allogeneic and autologous), increasing the likelihood of being cured.

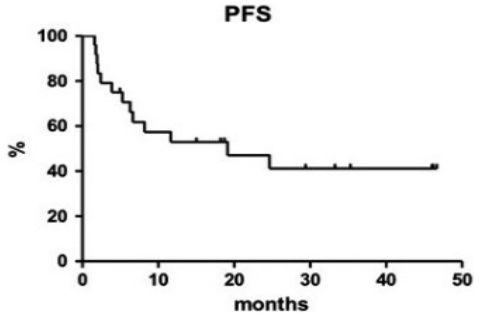


FIGURE 1 Progression-free survival with chemotherapy post checkpoint inhibitor therapy

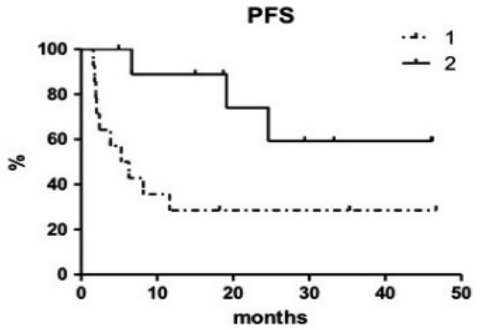


FIGURE 2 Progression-free survival with salvage treatment (1: single agent; 2: multi-agents regimen). Abbreviations: PFS, progression-free survival

RUOLO DELLA PET NEI LINFOMI

LINFOMA DI HODGKIN PET

Annals of Oncology 10: 1181–1184, 1999.

The role of positron emission tomography (PET) in the management of lymphoma patients

P. L. Zinzani,[1] M. Magagnoli,[1] F. Chierichetti,[2] M. Zompatori,[3] G. Garraffa,[2] M. Bendandi,[1] F. Gherlinzoni,[1] C. Cellini,[1] V. Stefoni,[1] G. Ferlin[2] & S. Tura[1]

Our study on a large number of patients with significant abdominal involvement (all with a mass of at least 5 cm and 41% of the patients presented bulky disease) provides definitive confirmation of PET's utility as a specific re-staging tool to assess the results of therapy and to diagnose the persistence of viable tumors in patients with abdominal residual masses and thus its validity in the follow-up of abdominal masses in these lymphomas.

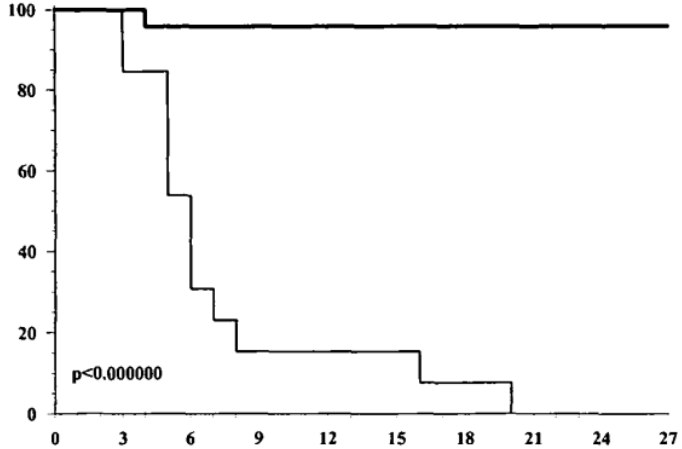


Figure 1. RFS curves of 37 patients with positive CT scan according to PET results (PET^+ (——), 13 patients ; PET^- (——), 24 patients).

LINFOMA DI HODGKIN PET

Annals of Oncology 17: 1296–1300, 2006

Early positron emission tomography (PET) restaging: a predictive final response in Hodgkin's disease patients

P. L. Zinzani[1]*, M. Tani[1], S. Fanti[2], L. Alinari[1], G. Musuraca[1], E. Marchi[1], V. Stefoni[1], P. Castellucci[2], M. Fina[1], M. Farshad[2], S. Pileri[1] & M. Baccarani[1]

Table 3. Comparison between PET-2 status and final clinical results

PET-2 status	No. of patients	Final clinical result (No. of patients)	
Positive	8	7 refractory 1 early relapse	100%
MRU	4	1 early relapse	25%
Negative	28	0 refractory/relapse	

MRU, minimal residual uptake.

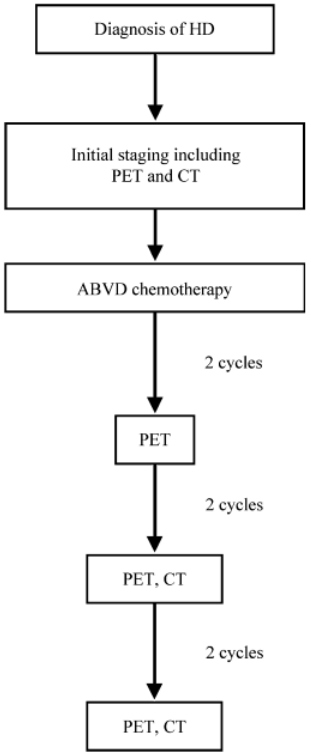


Figure 1. Flow-chart of the study.

The PET use for early (after two cycles) response assessment in HD patients is a significant step forward and has the potential to help physicians make crucial decisions about further treatment

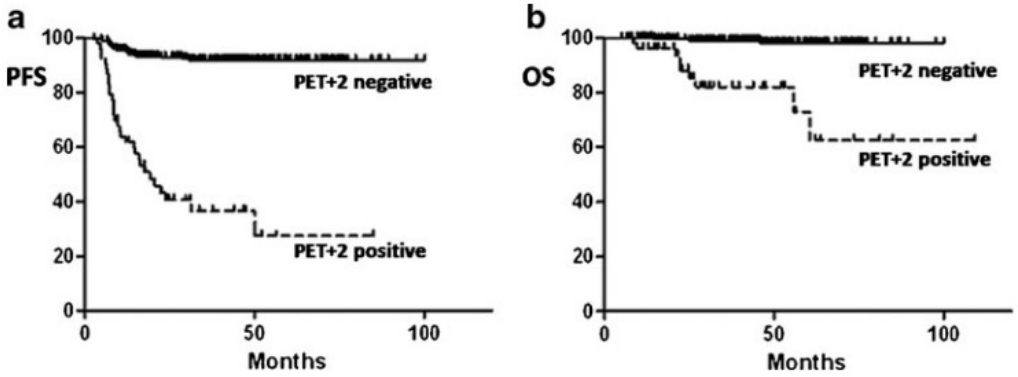
LINFOMA DI HODGKIN PET

Eur J Nucl Med Mol Imaging (2012)

Early interim ^{18}F-FDG PET in Hodgkin's lymphoma: evaluation on 304 patients

Pier Luigi Zinzani · Luigi Rigacci · Vittorio Stefoni · Alessandro Broccoli · Benedetta Puccini · Antonio Castagnoli · Luca Vaggelli · Lucia Zanoni · Lisa Argnani · Michele Baccarani · Stefano Fanti

Fig. 2 PFS (**a**) and OS (**b**) curves for the entire study population in relation to the PET+2 results



LINFOMA DI HODGKIN PET

VOLUME 34 · NUMBER 12 · APRIL 20, 2016

JOURNAL OF CLINICAL ONCOLOGY

Interim Positron Emission Tomography Response–Adapted Therapy in Advanced-Stage Hodgkin Lymphoma: Final Results of the Phase II Part of the HD0801 Study

Pier Luigi Zinzani, Alessandro Broccoli, Daniela Maria Gioia, Antonio Castagnoli, Giovannino Ciccone, Andrea Evangelista, Armando Santoro, Umberto Ricardi, Maurizio Bonfichi, Ercole Brusamolino,† Giuseppe Rossi, Antonella Anastasia, Francesco Zaja, Umberto Vitolo, Vincenzo Pavone, Alessandro Pulsoni, Luigi Rigacci, Gianluca Gaidano, Caterina Stelitano, Flavia Salvi, Chiara Rusconi, Monica Tani, Roberto Freilone, Patrizia Pregno, Eugenio Borsatti, Gian Mauro Sacchetti, Lisa Argnani, and Alessandro Levis

Patients with advanced-stage Hodgkin lymphoma for whom treatment was at high risk of failing appear to benefit from early treatment intensification with autologous transplantation, as indicated **by the possibility of successful salvage treatment in more than 70% of PET2-positive patients through obtaining the same 2-year progression-free survival as the PET2-negative subgroup.**

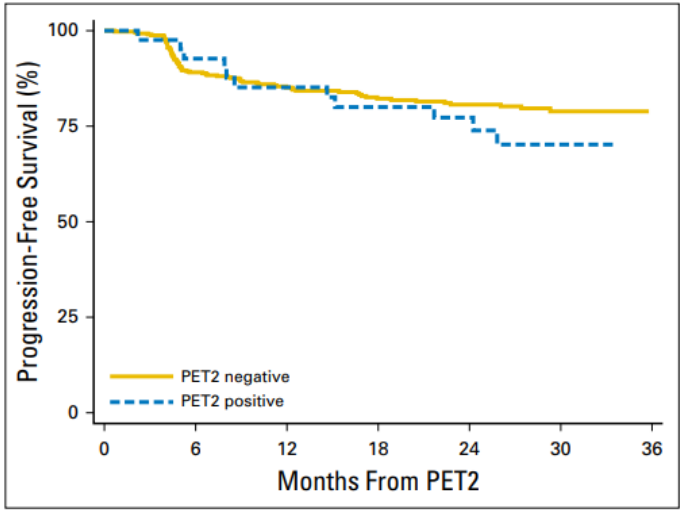


Fig 5. Progression-free survival on an intention-to-treat basis. Solid line, PET2-negative patients; dashed line, PET2-positive patients (Deauville score 4 and 5).

LINFOMI INDOLENTI

LINFOMA INDOLENTE FLUDARABINA

Annals of Oncology **4**: 575–578, 1993.

Fludarabine: An active agent in the treatment of previously-treated and untreated low-grade non-Hodgkin's lymphoma

P. L. Zinzani, F. Lauria, D. Rondelli, D. Benfenati, D. Raspadori, M. Bocchia, M. Bendandi
A. Gozzetti, F. Zaja[1] R. Fanin,[1] D. Russo,[1] P. Galieni[2] & S. Tura

In conclusion, on the basis of these data and those reported by other investigators, FLU as a single agent is associated with a significant response rate in relapsed and advanced LG-NHL patients…

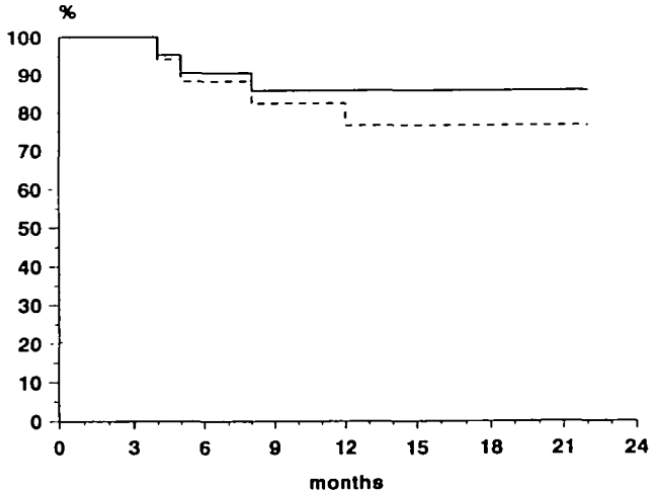


Fig. 1. The overall survival (——) and progression-free survival (– – –) curves of 21 LG-NHL patients treated with fludarabine.

LINFOMA INDOLENTE FLUDARABINA

Annals of Oncology **8**: 379–383, 1997.

Fludarabine–mitoxantrone combination-containing regimen in recurrent low-grade non-Hodgkin's lymphoma

P. L. Zinzani, M. Bendandi, M. Magagnoli, F. Gherlinzoni, E. Merla & S. Tura

- Of the 48 relapsed/refractory LG-NHL patients evaluated in this study for response to and toxic effects of the FMP regimen, we obtained an encouraging overall response rate of 83% with a CR rate of 35%.
- FMP was a relatively well-tolerated regimen with frequent mild toxic reactions characterized mainly by myelosuppression and infections.

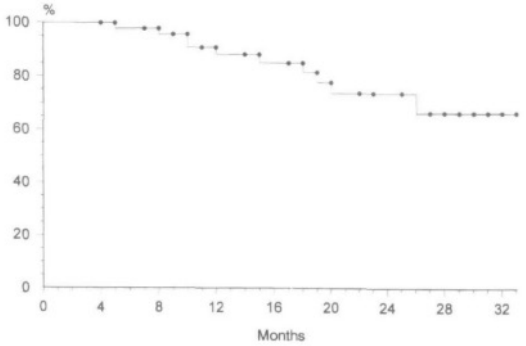


Figure 1. The overall survival curve of 48 recurrent LG-NHL.

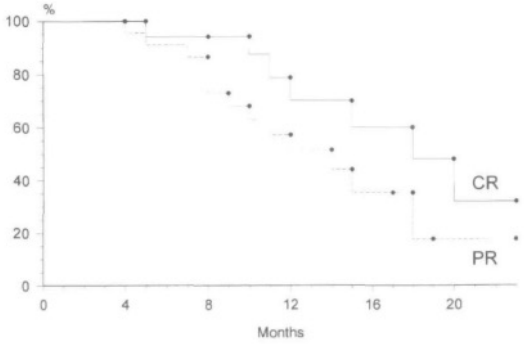


Figure 2. The relapse-free survival curves with respect to response.

LINFOMA INDOLENTE RITUXIMAB

Am. J. Hematol. 88:E273–E276, 2013.

Fludarabine-mitoxantrone-rituximab regimen in untreated intermediate/high-risk follicular non-Hodgkin's lymphoma: Experience on 142 patients

Pier Luigi Zinzani,* Cinzia Pellegrini, Alessandro Broccoli, Beatrice Casadei, Lisa Argnani, and Stefano Pileri

By comparison with the other competing chemothera-pies, our study confirmed an important percentage of CRs **higher than those obtained with CHOP-R, CVP-R, and BR** and an impressive DFS (also in termsof a median follow-up period) higher than those reportedfor the other chemoimmunotherapies

Regarding the utility of PET at the end of front-line che-moimmunotherapy, we reported that a positive PET could predict a significant shorter PFS.

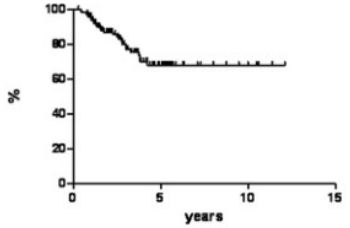


Figure 2. Progression-free survival.

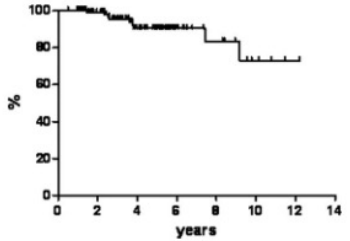


Figure 3. Overall survival.

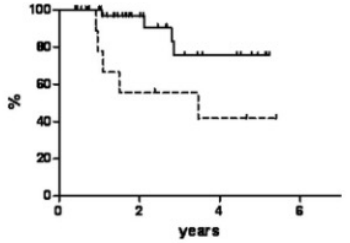


Figure 4. Progression-free survival: PET negative patients (continuous line) versus PET positive patients (dotted line) ($N = 56$, $P = 0.0024$).

LINFOMA INDOLENTE RITUXIMAB

VOLUME 22 · NUMBER 13 · JULY 1 2004

JOURNAL OF CLINICAL ONCOLOGY

Fludarabine Plus Mitoxantrone With and Without Rituximab Versus CHOP With and Without Rituximab As Front-Line Treatment for Patients With Follicular Lymphoma

Pier Luigi Zinzani, Alessandro Pulsoni, Alessio Perrotti, Simona Soverini, Francesco Zaja, Amalia De Renzo, Sergio Storti, Vito Michele Lauta, Luciano Guardigni, Patrizia Gentilini, Alessandra Tucci, Anna Lia Molinari, Marco Gobbi, Brunangelo Falini, Pier Paolo Fattori, Fabrizio Ciccone, Lapo Alinari, Maurizio Martelli, Stefano Pileri, Sante Tura, and Michele Baccarani

Our data lead us to propose FM as a more effective front-line chemotherapy strategy with respect to CHOP for routine first-line treatment of FL in terms of clinical (and molecular) response

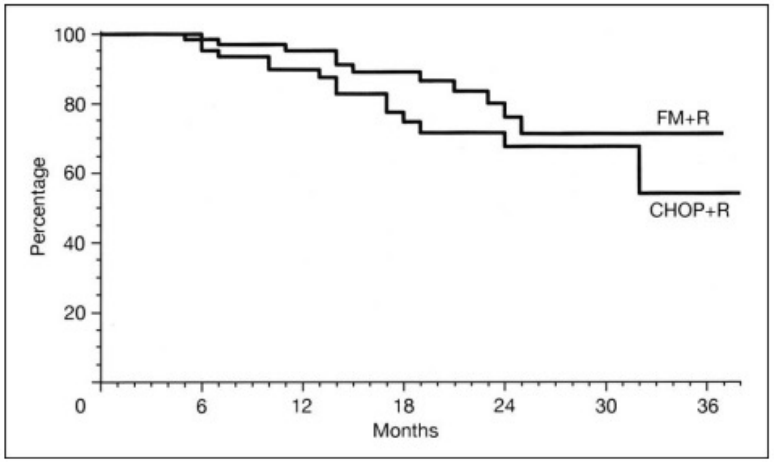


Fig 6. Progression-free survival curves of patients treated with fludarabine plus mitoxantrone (FM) + rituximab (R) and patients treated with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) + R.

IBRITUMOMAB TIUXETANO

CANCER February 15, 2008

A Phase 2 Trial of Fludarabine and Mitoxantrone Chemotherapy Followed by Yttrium-90 Ibritumomab Tiuxetan for Patients With Previously Untreated, Indolent, Nonfollicular, Non-Hodgkin Lymphoma

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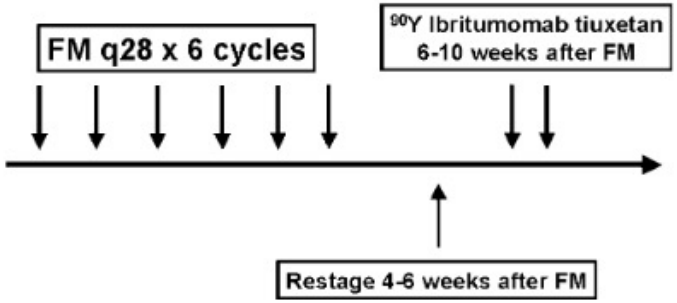

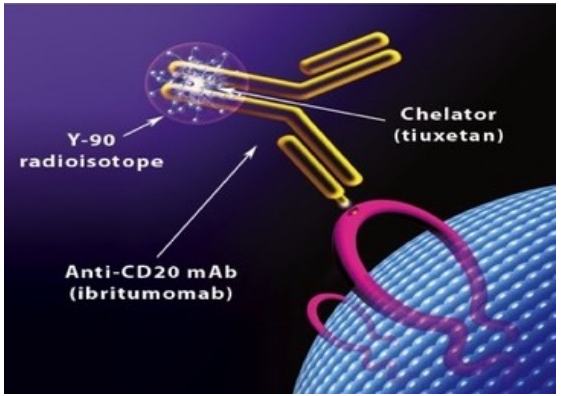

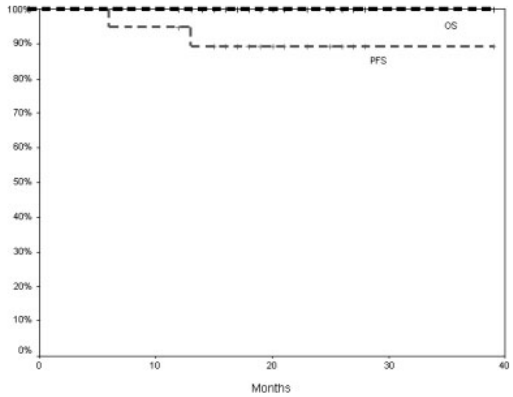

FIGURE 2. Overall survival (OS) and progression-free survival (PFS) curves of all 20 patients.

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Lancet Oncol 2008; 9: 352–358

Fludarabine and mitoxantrone followed by yttrium-90 ibritumomab tiuxetan in previously untreated patients with follicular non-Hodgkin lymphoma trial: a phase II non-randomised trial (FLUMIZ)

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In particular, the data represent the first evidence of a role of 90Y-ibritumomab tiuxetan after a fludarabine-containing regimen in the treatment of follicular NHL.

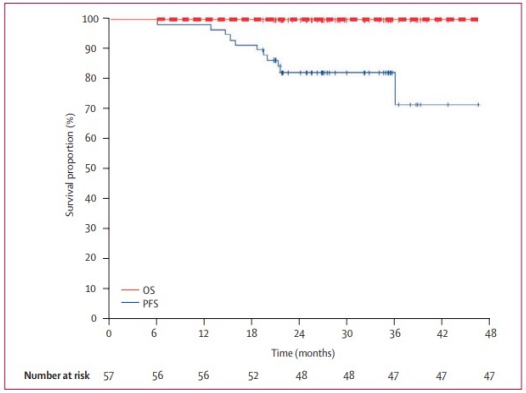
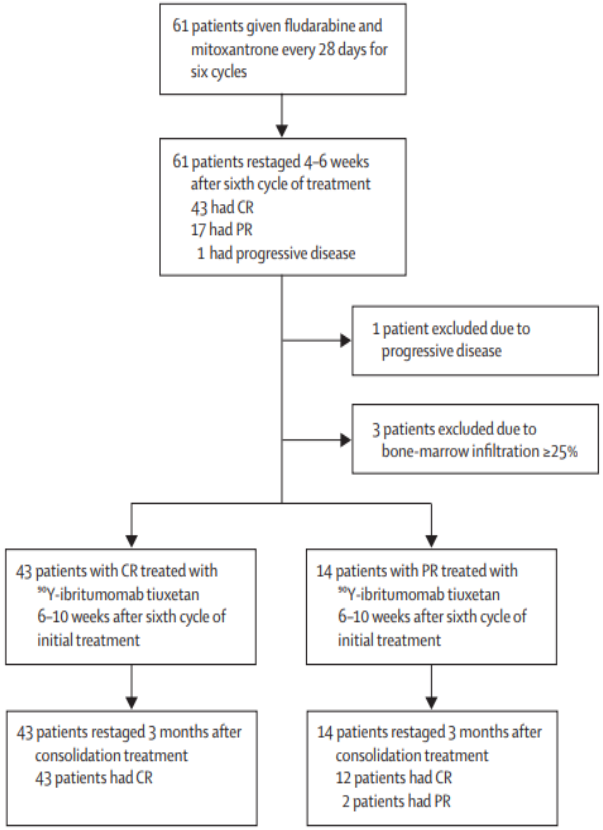


Figure 2: Kaplain-Meier curves for overall survival and progression-free survival after treatment with fludarabine and mitoxantrone followed by ^{90}Y-ibritumomab tiuxetan in untreated patients with follicular NHL



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Oncotarget, 2018, Vol. 9, (No. 34),

Research Paper

Italian real life experience with ibrutinib: results of a large observational study on 77 relapsed/refractory mantle cell lymphoma

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In conclusions, thrombocytopenia, diarrhea and lung infections are the relevant adverse events to be clinically focused on; regarding effectiveness, ibrutinib is confirmed to be a valid option for refractory/relapsed MCL also in a clinical setting mimicking the real world.

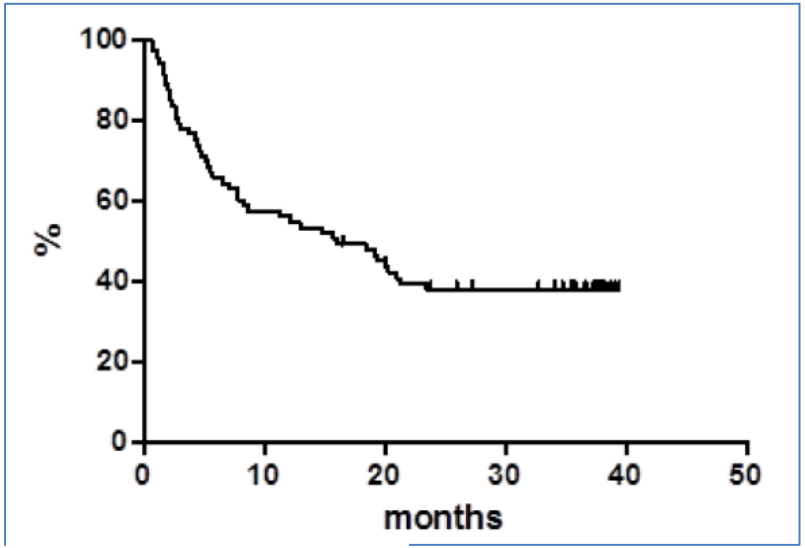

Figure 1: Overall survival.

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The MAGNOLIA Trial: Zanubrutinib, a Next-Generation Bruton Tyrosine Kinase Inhibitor, Demonstrates Safety and Efficacy in Relapsed/Refractory Marginal Zone Lymphoma

Stephen Opat[1], Alessandra Tedeschi[2], Kim Linton[3], Pamela McKay[4], Bei Hu[5], Henry Chan[6], Jie Jin[7], Magdalena Sobieraj-Teague[8], Pier Luigi Zinzani[9,10], Morton Coleman[11], Catherine Thieblemont[12,13], Peter Browett[14], Xiaoyan Ke[15], Mingyuan Sun[16], Robert Marcus[17], Craig A. Portell[18], Kirit Ardeshna[19,20], Fontanet Bijou[21], Patricia Walker[22], Eliza A. Hawkes[23,24,25], Sally Mapp[26,27], Shir-Jing Ho[28], Dipti Talaulikar[29], Ke-Shu Zhou[30], Melannie Co[31], Xiaotong Li[32], Wenxiao Zhou[32], Massimo Cappellini[31], Chris Tankersley[31], Jane Huang[31], and Judith Trotman[33]

Zanubrutinib was effective in patients with R/R MZL as demonstrated by high ORR and CR rates, which compares favorably with the currently marketed therapies (ibrutinib, lenalidomide plus rituximab, and umbralisib) and investigational (copanlisib and parsaclisib) agents for MZL

Responses were durable and generally consistent across MZL subtypes and difficult-to-treat subgroups.

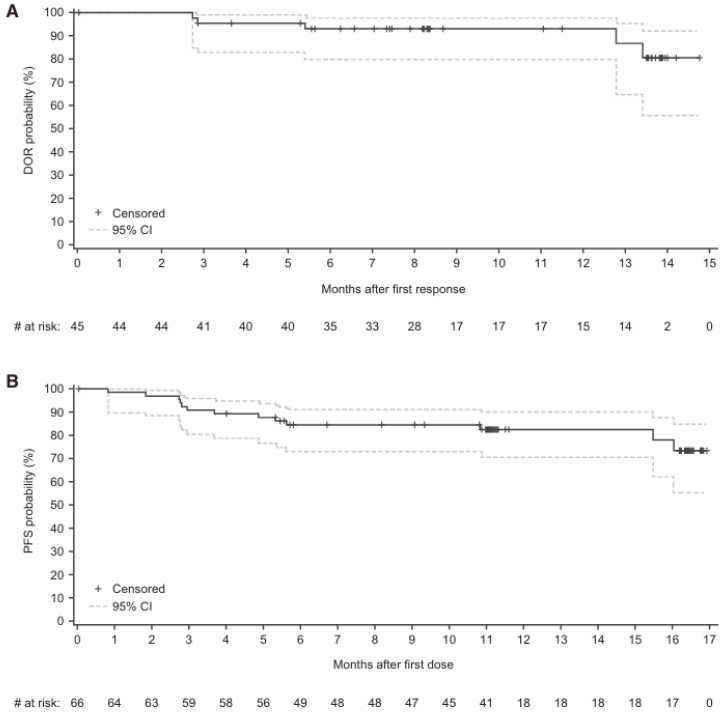

Figure 1.
A, Kaplan–Meier plot of duration of response with zanubrutinib per IRC assessment based on Lugano classification (15) for patients with MZL in the MAGNOLIA study (BGB-3111–214). Only patients with either PR or CR were included. **B,** Kaplan–Meier plot of PFS with zanubrutinib per IRC assessment based on Lugano classification (15) for patients with MZL in the MAGNOLIA study (BGB-3111–214). CIs were calculated using a generalized Brookmeyer and Crowley method.

Attualmente sono in corso 30 studi sperimentali GCP (FASE I-II-III-IV) rivolti a pazienti affetti da Linfoma di Hodgkin e Linfoma indolente.