Kompetenznetz Maligne Lymphome

Lymphom Kompetenz KOMPAKT

KML-Experten berichten

16th ICML 2021 Virtual

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Klinik I für Innere Medizin | Uniklinik Köln

Hodgkin Lymphom

Offenlegung potentieller Interessenskonflikte

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Other financial relationships	–
Intangible conflicts of interest	–

Kapitel 1

RELAPSES IN INTERIM PET NEGATIVE LIMITED STAGE HODGKIN LYMPHOMA PATIENTS RECEIVING ABVD WITH OR WITHOUT RADIOTHERAPY–ANALYSIS OF EORTC/FIL/LYSA H10 AND UK NCRI RAPID TRIALS

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Introduction

- Randomized trials H10 and RAPID were designed to assess whether radiotherapy can be safely omitted in newly diagnosed limited-stage Hodgkin lymphoma patients who are interim PET-negative after 2 (HD10) or 3 (RAPID) cycles of ABVD.
- In both studies relapses were more frequent after chemotherapy only than after combined modality treatment.
- *A recent exploratory analysis of the H10 study showed that most relapses after chemotherapy only occurred in the first 2 years after treatment and were observed in initially involved areas. Male sex and stage II were negative prognostic factors in H10.*

➢ The presented study analyzed the independent data set of the RAPID trial to investigate wether the HD10 data set findings can be replicated.

Results

		F		U		Unclassified*	
		C+RT	C	C+RT	C	C+RT	C
H10	randomized	227	238	292	302	0	0
	relapsed	2 (1%)	30 (13%)	16 (5%)	30 (10%)	0	0
RAPID	randomized	118	123	65	63	25	25
	relapsed	6 (5%)	13 (11%)	3 (5%)	5 (8%)	0	3 (12%)

*mainly due to missing ESR.

TABLE 1 Number, group allocation and outcome of patients randomized in the H10 and RAPID trials

- The low number of relapses in the U group prevented a reliable comparison with the H10 counterpart.
  - ➢ The effect of gender and stage went in the same direction as in H10 but was non-significant.
- In a second step H10 and RAPID (F+U groups) were combined in a Cox model stratified by study, with a different HR before and after 2 years.
  - ➢ In the combined analysis, the hazard of relapses was significantly lower after C+RT than after C during the first 2 but similar from 2 years onwards.

Conclusion

- The independent validation with RAPID and the combined analysis **confirm the H10 finding** that omitting RT in interim PET neg. patients treated with chemotherapy results in an increase in early relapses more frequently confined to initially involved areas.

- GHSG perspective: this analysis confirms our published finding from our HD16 study, showing the importance of IS-RT for definitive lymphoma control and supports its definition as SOC in early favourable stage HL.

Kapitel 2

PET ADAPTED THERAPY IN BULKY STAGE I/II CLASSIC HODGKIN LYMPHOMA (CHL)

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Introduction

- Bulky disease is associated with inferior outcomes in patients with early stage cHL.
- The authors investigated a PET-adapted approach to reduce the need for RT in patients with PET2-negative (PET-) disease and escalate therapy in patients with PET2-positive (PET+) disease.
- 101 patients enrolled, primary endpoint: progression-free survival (PFS) estimated from PET2.

Methods:

- Eligible patients aged 18-60 years had stage IA-IIB cHL with disease bulk > 10 cm or > .33 max intrathoracic diameter on chest x-ray.
- Patients received 2 cycles of doxorubicin-bleomycin- vinblastine-dacarbazine (ABVD) followed by centrally reviewed PET. PET negative was defined as Deauville of 1-3.
  - PET2- patients received 4 additional cycles of ABVD.
  - PET2+ patients received 4 cycles of eBEACOPP plus 30 Gy involved site RT

PET ADAPTED THERAPY IN BULKY STAGE I/II CLASSIC HODGKIN LYMPHOMA (CHL)

Characteristic	Total n=94	PET2 negative n=73	PET2 positive n=21	P value
Female Sex, n (%)	50 (53)	41 (56)	9 (43)	0.33
Age median (range)	30 (18-58)	30 (18-58)	28 (19-56)	0.39
Stage, n (%)				0.78
IA/IAE	7 (7)	6 (8)	1 (5)	
IB	2 (2)	2 (3)	0 (0)	
IIA/IIAE	37 (39)	30 (41)	7 (33)	
IIB/IIBE	48 (51)	35 (48)	13 (62)	
ECOG PS, n (%)				0.14
0	64 (68)	52 (71)	12 (57)	
1	29 (31)	21 (29)	8 (38)	
2	1 (1)	0 (0)	1 (5)	
Prior ABVD, n (%)	15 (16)	13 (18)	2 (10)	0.51

PET ADAPTED THERAPY IN BULKY STAGE I/II CLASSIC HODGKIN LYMPHOMA (CHL)

Hematologic/Infectious Toxicity

PET2 negative
ABVD x 6 (78%)

Adverse Event	Any grade	Grade 3	Grade 4
Neutrophils	68 (93%)	9 (12%)	54 (74%)
Platelets	6 (8%)	1 (1%)	1 (1%)
F+N	6 (8%)	6 (8%)	0 (0%)
Sepsis	0 (0%)	0 (0%)	0 (0%)

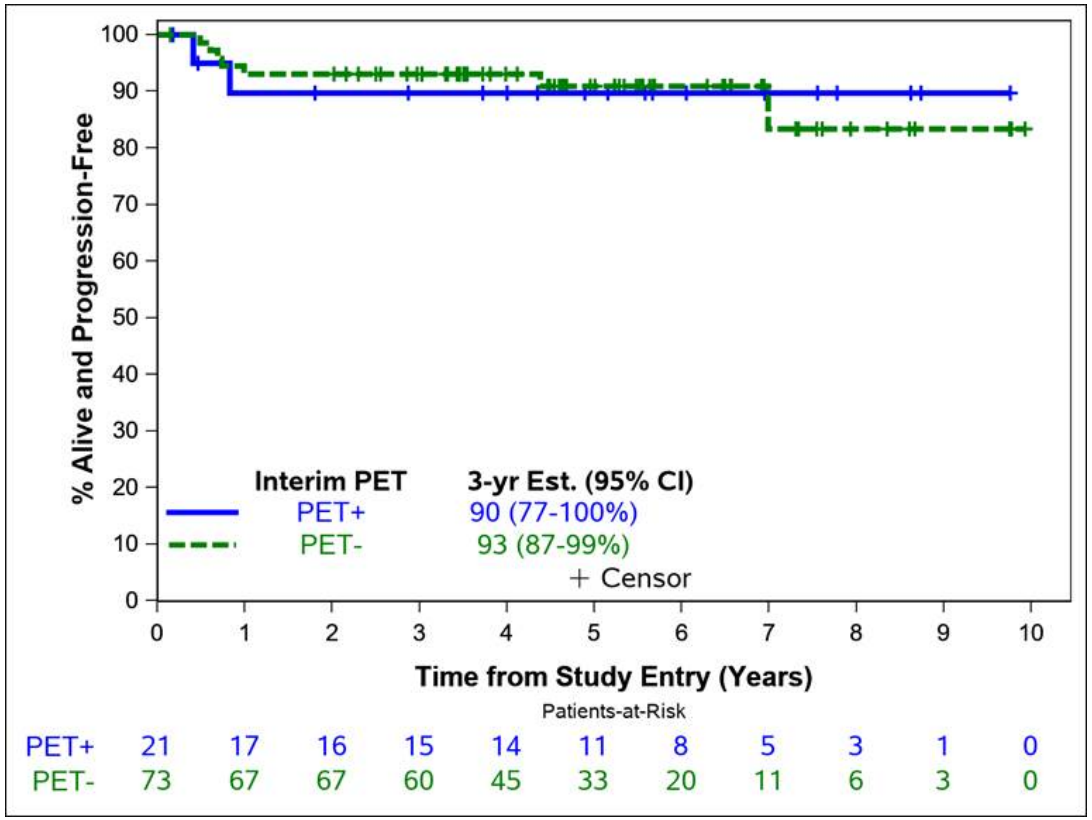
PET2 positive
ABVD x 2/BEACOPP x 4 + RT (22%)

Adverse Event	Any grade	Grade 3	Grade 4
Neutrophils	21 (100%)	6 (29%)	12 (57%)
Platelets	15 (71%)	3 (14%)	3 (14%)
F+N	2 (10%)	2 (10%)	0 (0%)
Sepsis	1 (5%)	0 (0%)	1 (5%)

Ann S. LaCasce, MD, MMSc

PET ADAPTED THERAPY IN BULKY STAGE I/II CLASSIC HODGKIN LYMPHOMA (CHL)

- PET2- patients 3-yr PFS estimates:
  93.1% (95% CI: 87.4-99.1%)
- PET2+ patients 3-yr PFS estimates:
  89.7% (95% CI: 77.2-100.0%)
- All patients 3-yr PFS estimates:
  92.3% (95% CI: 87.0-98.0%)



Conclusions

- Excellent PFS outcomes were observed in all patients using a PET-adapted approach that allowed omission of RT in 78% of patients.
- PET2+ patients treated with eBEACOPP and consolidative RT did not have inferior outcomes.

GHSG perspective:

- This is a mixture of unfavourable and advanced stage disease in a phase II study without standard group and a very small sample size:
  - ➢ stand alone data, non-randomized, hardly to compare to any other trial, conflicting results (H10!): hardly to put into perspective
- GSHG strategy allows treatment with much less intensive therapy for all stages!

Kapitel 3

NIVOLUMAB FOR RELAPSED OR REFRACTORY (R/R) CLASSICAL HODGKIN LYMPHOMA (CHL) AFTER AUTOLOGOUS TRANSPLANTATION: 5-YEAR OVERALL SURVIVAL FROM THE PHASE 2 CHECKMATE 205 STUDY

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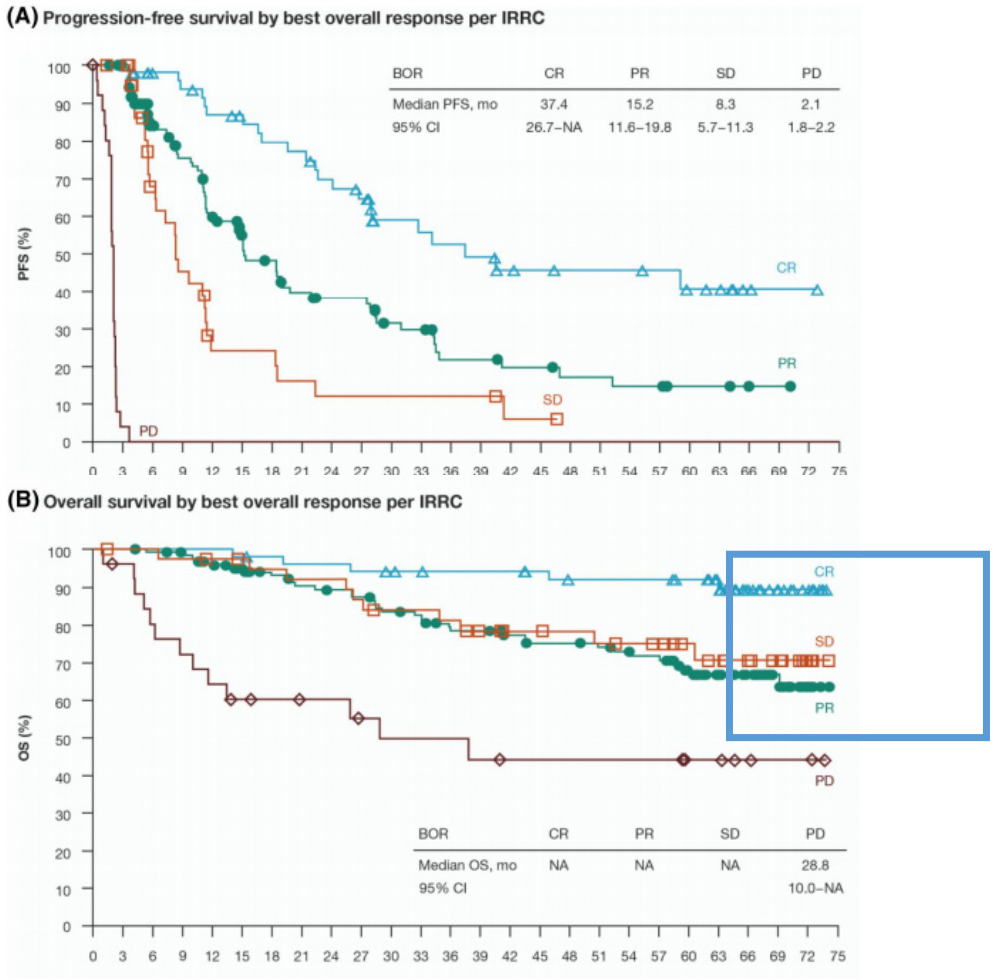
Introduction

- CheckMate 205 (NCT02181738), a study in pts with **R/R cHL** treated with **Nivolumab (NIVO)** after autologous hematopoietic cell transplantation (auto-HCT)[1] demonstrated
  - ORR of 69%,
  - median DOR of 17 mo
  - median PFS of 15 mo
- median FU of initial report was 18 mo, now updated results after **median FU of 58 mo**

1. Armand P et al : Nivolumab for Relapsed/Refractory Classic Hodgkin Lymphoma After Failure of Autologous Hematopoietic Cell Transplantation: Extended Follow-Up of the Multicohort Single-Arm Phase II CheckMate 205 Trial. J Clin Oncol. 2018 May

5-YEAR OVERALL SURVIVAL FROM THE PHASE 2 CHECKMATE 205 STUDY

- 243 pts were treated, m**edian PFS was 15 mo (CI95: 11– 19), and** median DOR was 18 mo (CI95: 15–26).
- CR vs PR : longer median PFS (37 vs 15 mo) and DOR (30 vs 13 mo)
- **The 2-y and 5-y PFS rates (CI95): 37% (30–44) and 18% (12–25), respectively.**
- The 2-y and 5-y OS rates (CI95): 87% (82–91) and 71% (65–77),
- **12 pts stopped study Tx after ≥ 1 y of CR per protocol (Cohort C).**
  - **6 pts still in response;**
  - **3 were re-treated with NIVO (-> 2 CR and 1 PR).**
- **No new toxicities were observed,**
- Grade 3–4 TRAEs occurred in 68 pts (28%) & led to discontinuation in 26 pts (11%).
- no Tx-related deaths.



5-YEAR OVERALL SURVIVAL FROM THE PHASE 2 CHECKMATE 205 STUDY: conclusions

- Five-year analysis of CheckMate 205 cohorts ABC confirms the **efficacy and safety of NIVO** for pts with **cHL who progressed or relapsed after auto-HCT**.
- Safety profile is similar to previous reports.
- It appears feasible to stop NIVO after 1 y of CR and re-initiate tx upon disease progression.

Haben Sie Fragen zu diesem Thema?

Schreiben Sie uns!

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Die Kurzpräsentationen sind online unter

www.lymphome.de/icml2021

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