Abstract V456:

Nivolumab in Kombination mit Gemcitabine und Oxaliplatin (GemOx) bei rezidivierten/refraktären T-Zell Lymphomen: vorläufige Ergebnisse des experimentellen Arms der Niveau Studie

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Interessenskonflikte:

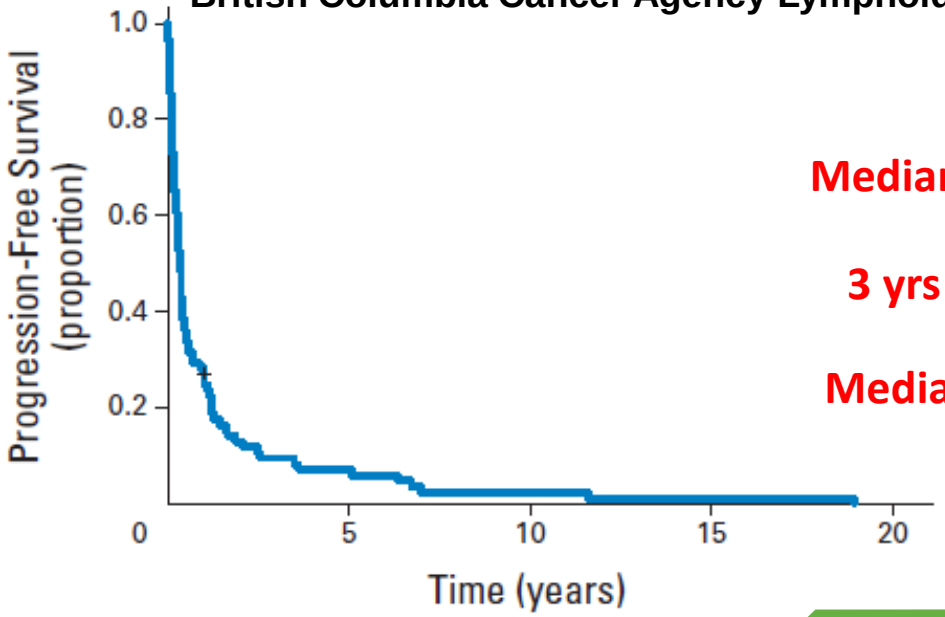
Forschungsunterstützung:
BMS, Acrotech Biopharma LLC, Roche, Amgen

Vortragstätigkeit:
BMS, Roche, MSD

Beratertätigkeit:
BMS, Roche, MSD

Peripheral T cell Lymphoma – Prognosis after 1st relapse or progression

British Columbia Cancer Agency Lymphoid Cancer database:



Median PFS 3.7 months

3 yrs PFS 11%

Median OS 6.5 months

Mak, JCO, 2013

Key-Eligibility criteria

- First relapse or progression
- Aggressive Lymphoma (T- or B-cell origin)

- Ineligible for highdose chemotherapy defined as:
  - Age > 65 years and/or
  - HCT-CI score > 2
  - Relapse after autologous transplantation and ineligible for allogeneic transplantation

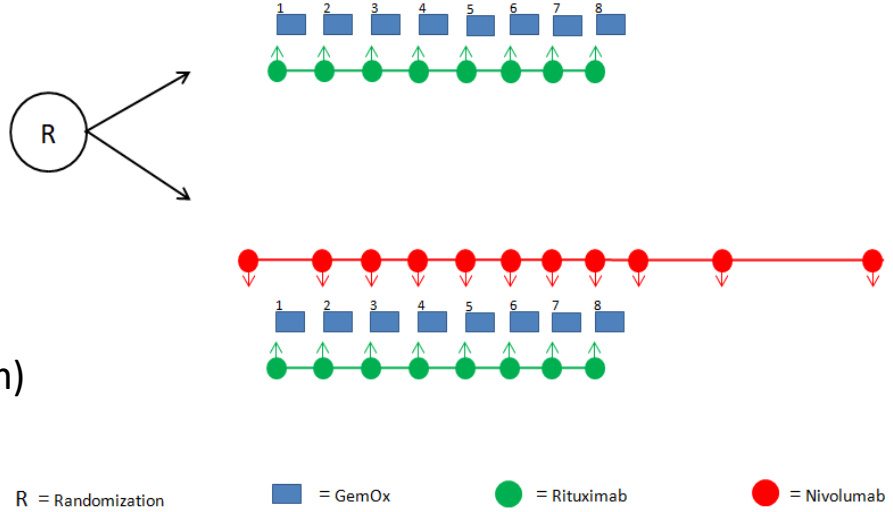
- Patients must have only one prior chemotherapy regimen including an anthracycline. Rituximab must be part of the first-line regimen in case of a $CD20^+$ lymphoma.
- …

Statistics and Design

Aggressive B cell lymphoma:

- Aim: 1-years PFS **27%** -> **42%**.
- Power 80%, alpha error 5% (two sided)

- Sample size calculation: 292 B-NHL patients,
- 5% drop-out -> **310 B-NHL patients** (155 in each arm)



peripheral T cell lymphoma:

- in parellel a maximum of **78 patients** with T cell lymphome will be included and randomized
- Based on observed efficacy and possible further increasing scientific knowledge an decision will be made to amend the trial:
- -> **Testing the main objective also in T cell lymphoma**

Westpfalz-Klinikum GmbH

Lysa

HOVON

Polish Lymphoma Research Group

AGMT ARBEITSGEMEINSCHAFT MEDIKAMENTÖSE TUMORTHERAPIE

CLSG KLS Czech Lymphoma Study Group Kooperativní lymfomová skupina

GLA German Lymphoma Alliance

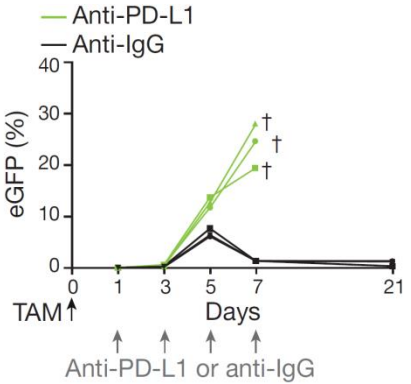
LETTER

doi:10.1038/nature24649

PD-1 is a haploinsufficient suppressor of T cell lymphomagenesis

Tim Wartewig[1,2], Zsuzsanna Kurgyis[1,2], Selina Keppler[1,2], Konstanze Pechloff[1,2,3], Erik Hameister[1,2], Rupert Öllinger[2,4], Roman Maresch[2,4], Thorsten Buch[5], Katja Steiger[6], Christof Winter[1,2,3], Roland Rad[2,3,4] & Jürgen Ruland[1,2,3,7]

***ITK-SYC$^{CD4\text{-}cre}$* mice**



Hyperprogressions in Nivolumab-monotherapy Phase-II trial

Is Nivolumab in combination with chemotherapy safe?

Bennani, ASH 2019 abstract #467 *Wartewig, Nature 2017*

Characteristics of first patients treated with Nivolumab – GemOx

	n=12 (%)
Median age, year (range)	69.5 years (53-80)
Baseline ECOG PS, n (%)	
0-1	9 (75%)
2	3 (25%)
Prior Auto-SCT, n (%)	2 (17%)
Refractory to first line therapy	5 (42%)
Stage of disease at enrollment	
I-II	1 (8%)
III-IV	11 (92%)
>1 extra-nodal site at enrollment, n (%)	7 (58%)
B-symptoms at enrollment, n (%)	2 (17%)
LDH > ULN at enrollment, n (%)	4 (33%)

Outcome - 1

	Patients (N=12)
No of GemOx cycles received (median, range)	6 (1-8)
No of NIV cycles received (median, range)	8 (1-26)
Premature treatment discontinuation	10 (7 during induction and 3 during consolidation)
Reasons for premature treatment discontinuation	7 lymphoma progression, 2 toxicity and 1 intercurrent disease

as of Sept. 20th, 2021

Outcome - 2

	Patients (N=12)
Overall response	9 (75%)
Complete remission	4 (33%)
Partial remission	5 (42%)
Primary progression	2
Hyperprogression*	0
Median PFS after Nivo-GemOx (PFS2)	6.9 months (95% CI: 0.3-13.5)
Median OS[&]	15.8 months (95% CI: 0–33.3)

*defined by Champiat S, et al. Hyperprogressive disease is a new pattern of progression in cancer patients treated by anti-PD-1/PD-L1. Clin. Cancer Res. 172 2017;23(8):1920–1928.

[&]After a median follow-up of 38.5 months, 10 patients have died (7 from lymphoma, 2 from infection (1 COVID-19 infection and 1 yeast septicemia) and 1 due to salvage therapy), and 2 remain alive.

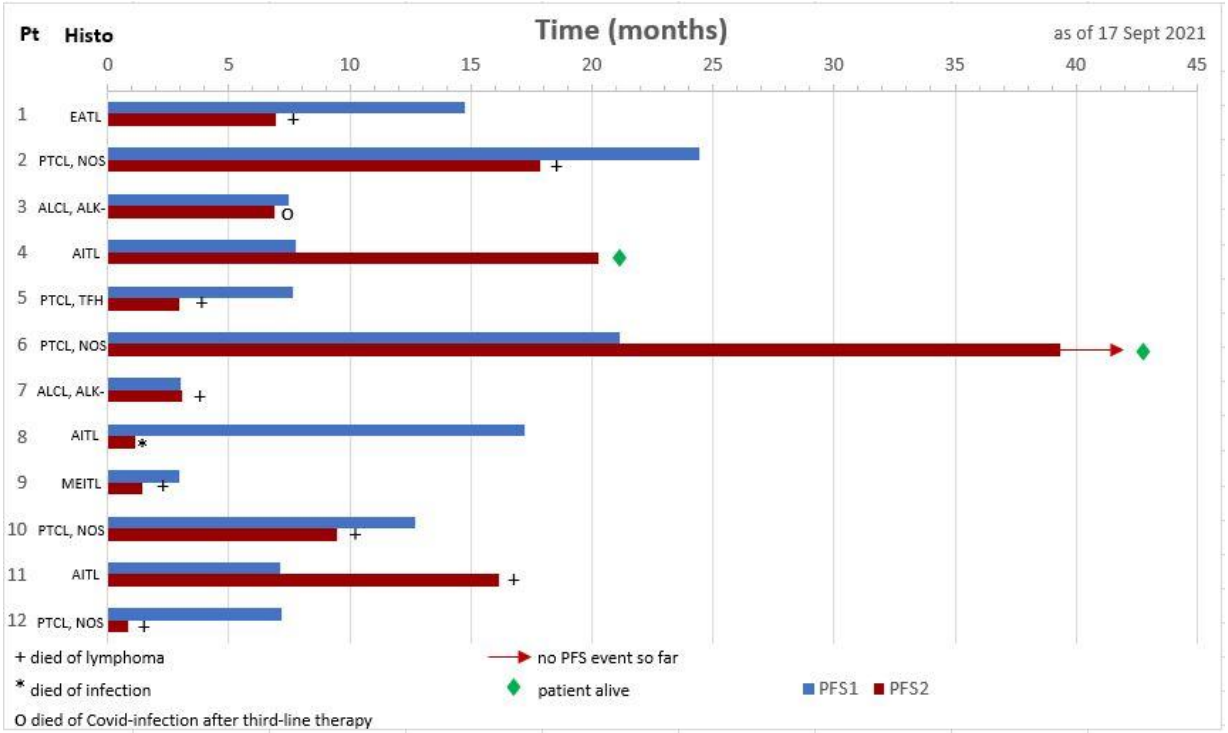
as of Sept. 20th, 2021

Outcome 3 - Response

	PD1 expression on tumor cells (%)	PD-L1 expression on tumor cells (%)	response
Enteropathy-associated T-cell lymphoma (EATL)	0	0	PR
Peripheral T-cell lymphoma, NOS (PTCL-NOS)	<10	0	CR
Anaplastic large cell lymphoma, ALK-negative (ALK- ALCL)	0	>75	PR
Angioimmunoblastic T-cell lymphoma (AITL)	>75	0	CR
Nodal peripheral T-cell lymphoma with TFH phenotype	0	0	PR
Peripheral T-cell lymphoma, NOS*	NA	NA	CR
Anaplastic large cell lymphoma, ALK-negative*	0	>75	PR
Angioimmunoblastic T-cell lymphoma	>75	0	SD
Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)	0	0	PD
Peripheral T-cell lymphoma, NOS	<10	0	CR
Angioimmunoblastic T-cell lymphoma	>75	0	PR
Peripheral T-cell lymphoma, NOS	75	0	PD

as of Sept. 20th, 2021

Outcome 4 - PFS1 vs PFS2



PFS1:
time from diagnosis to 1st relapse/progression.

PFS2:
time from randomisation to 2nd relapse/progression or death.

as of Sept. 20th, 2021

Toxicity

	Patients (N=12)	
AEs, Grade 3-4	**12 (100%)**	
AEs, Events Grade 5	**1 (8%)**	yeast septicemia
Immune related AEs, Induction (n=12)	**Grade 1-4**	**Grade 3-4**
Cerebral vasculitis	**1**	**1**
Diarrhea	6	-
Rash	2	-
Lipase increased	7	-
Amylase increased	6	-
Hypothyreodism	5	-
Immune related AEs, Consolidation (n=6)		
Diarrhea	1	-
Lipase increased	3	-
Amylase increased	2	-
Arthralgia	1	-

as of Oct. 16th, 2021

Conclusions:

- **Nivolumab-GemOx is safe without hyperprogressions.**
- **However, a scientific definition for hyperprogression is warranted.**
- **Nivolumab-GemOx demonstrates encouraging response rates.**
- **PFS2 vs. PFS1 suggests, that in some patients study therapy might be more effective than CHOP-based 1st-line therapy.**
- **Translational research program is obliged to define predictive biomarkers.**
- **Findings will have to be confirmed on a larger number of patients by comparing with the control arm (Gem-Ox) once the NIVEAU study will be completed.**