Phase I clinical trials: a retrospective analysis from a single center

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** Presenter*

Introduction

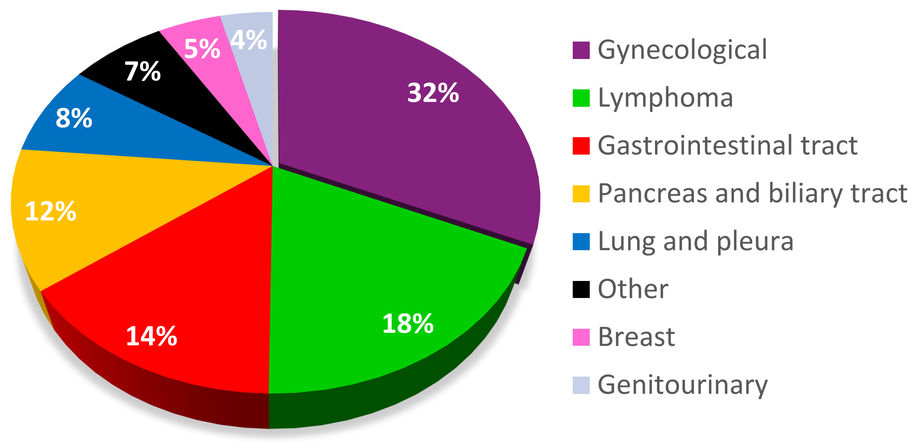
- Phase I trials represent the first step in the clinical evaluation of a new drug or new combination
- Main objective is determination of safety and recommended phase II dose
- Traditionally regarded as pharmacological trials with small benefit for patients
- Recent improvements in drug development have improved response rates
- We did a retrospective analysis of main outcomes for patients participating in phase I clinical trials at the Oncology Institute of Southern Switzerland (IOSI)

Patients and methods

- **Study design and population**: retrospective single center analysis in patients with solid tumor or lymphoma, enrolled in phase I trials or phase I portion of phase I/II clinical trials at the IOSI between January 2012 and December 2021
- **Objectives**: evaluate outcome (safety and efficacy)
- **Variables taken in consideration:** demographics, ECOG performance status, body mass index, baseline hematology and chemistry, disease characteristics including genetic alterations, prior local and systemic therapies, type of trial treatment
- **Endpoints**: treatment related deaths, dose limiting toxicities (DLTs), dose delays and dose reductions, complete remission (CR), partial remission (PR), stable disease (SD), progressive disease (PD) and overall response rate (ORR: CR+PR)
- **Statistical analysis:** performed with STATA 16 software package
  - Chi-square test or the Fisher's exact test used for testing associations
  - Univariate analysis performed by logistic regression with response status (yes or no) as independent variable, backward logistic regression used for multivariate analysis of response
  - Significance level set at $p < 0.05$ for all tests

Results

Figure 1. Baseline characteristics (n=255 patients, participating in 40 trials)



Of all patients, 92% received previous systemic treatment, 8% were systemic-treatment naïve.
The median number of prior systemic treatment was 2, with a range of 0-11.

Table 1. Type of trial treatment

Phase I trial treatment		
Combination	145	(56.9)
Single agent	110	(43.1)
Non-genome/protein matched trial	184	(72.2)
Genome matched	71	(27.8)
Monotherapy		
Small molecule	58	(22.7)
Monoclonal antibody	35	(13.7)
Chemotherapy	16	(6.3)
Antibody-drug conjugate	1	(0.4)
Type of combination		
Non-chemo based	166	(65.1)
Chemo based	89	(34.9)

Table 2. Safety

Grade 5 adverse events	0	
DLT	38	(14.9)
Type of DLT (N=38)		
Non-hematological	24	(63.2)
Hematological	13	(34.2)
Both	1	(2.6)
Dose delay due to TRAEs*	108	(42.4)
Dose reduction due to TRAEs*	57	(22.4)

Figure 2. Response to therapy

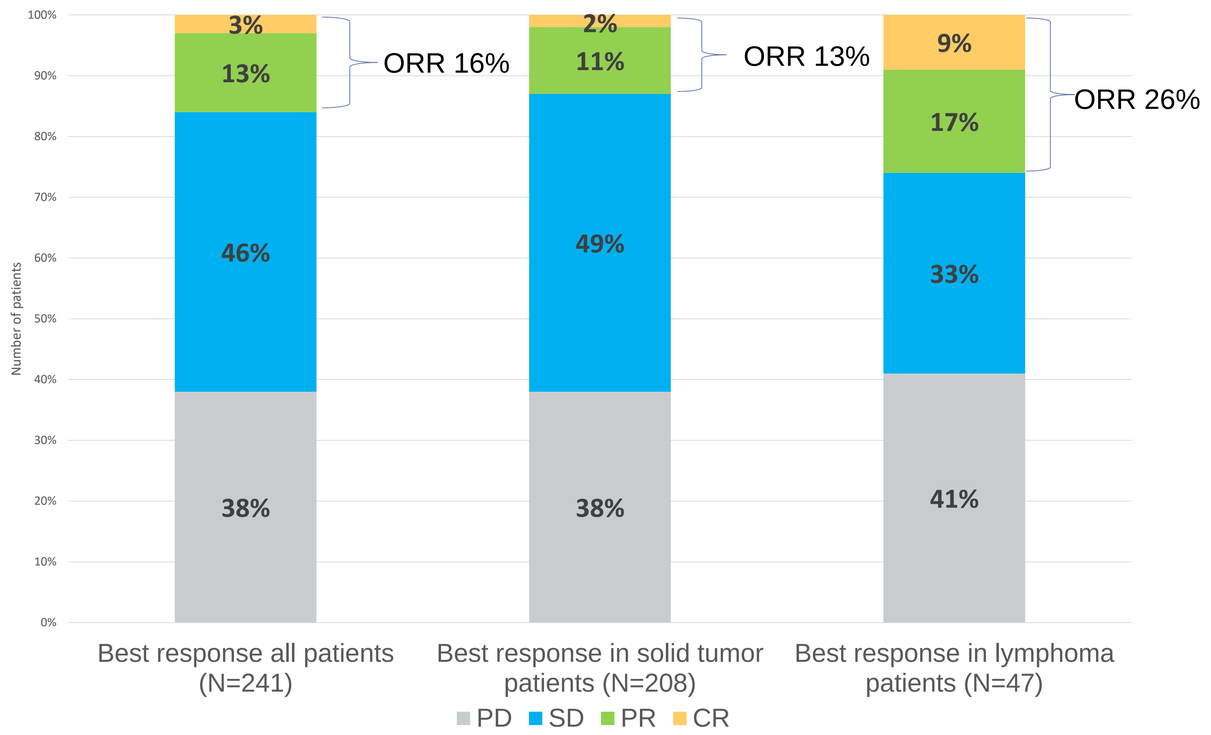


Table 3. Features asscoiated with respose to therapy at univariate analysis

	Fisher exact test		Logistic regression	
Variable	**ORR**	**P-value**	**Odds Ratio (95% CI)**	**P-value**
Neoplasia				
Gynecologic cancer vs. other types	22% vs 11%	0.037	2.2 (1.09-4.43)	0.027
Non-Hodgkin Lymphoma vs. solid tumors	25% vs 12%	0.039	2.4 (1.11-5.20)	0.027
Chemonäive vs. Pretreated	38% vs 12%	0.001	4.50 (1.92-10.55)	0.001
Number of prior system treatments (vs. untreated)				
Untreated	43%	0.006		1
1 line	11%		0.16 (0.05-0.54)	0.003
2 to 4 lines	14%		0.22 (0.08-0.60)	0.003
>4 lines	9%		0.013 (0.03-0.50)	0.003
Tumor extension				
Stage IV vs. stage III vs. stage II	12% vs 28% vs 67%	0.006	0.32 (0.16-0.65)	0.002
Metastatic vs. non-metastatic disease	12% vs 31%	0.006	0.31 (0.14-0.68)	0.004
Multiple metastatic sites vs. single	12% vs 25%	0.014	0.39 (0.19-0.81)	0.011
Type of phase-1 trial				
"Chemo-free" vs. Chemotherapy-based	9% vs 22%	0.003	0.33 (0.16-0.68)	0.003
Combo vs. single agents	23% vs 5%	<0.001	6.19 (2.33-16.45)	0
Genome/protein-matched vs. non-matched	4% vs 19%	0.003	0.19 (0.006-0.63)	0.007

Table 4. Multivariate analysis: variables correlating with response (model 1)

Variable	Odds Ratio	SE	P-value	95% CI
Neoplasia				
Gynecologic cancer vs. other types	**3.57**	**1.80**	**0.012**	**1.32-9.62**
Non-Hodgkin Lymphoma vs. solid	**3.23**	**1.92**	**0.047**	**1.02-10.38**

Table 5. Multivariate analysis: variables correlating with response (model 2)

Variable	Odds Ratio	SE	P-value	95% CI
Neoplasia				
Gynecologic cancer vs. other types	**3.45**	**1.80**	**0.018**	**1.24-9.61**
Non-Hodgkin Lymphoma vs. solid	**4.26**	**2.85**	**0.030**	**1.15-15.78**
Type of phase-1 trial				
Combo vs. single agents	**4.91**	**3.12**	**0.012**	**1.42-17.04**

Model 1: includes patients demographic/clinical characteristics and tumor burden parameters.
Model 2: includes patients demographic/clinical characteristics, tumor burden parameters, and phase-I trials features

Conclusions

- Phase I trials were safe and no treatment-related deaths were observed
- 13% of patients with solid tumor and 26% of patients with lymphoma responded to therapy
- Results are consistent with data recently published
- Phase I trials represent a valuable treatment option for patients with advanced solid tumor or lymphoma

Contacts and Disclosure

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Authors of this poster have no conflict of interest to declare