Clinical trial design in the era of precision oncology: an overview of the last 20 years

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BACKGROUND

The recent advent of the "precision oncology" model changed the face of modern drug development. The chance of quickly carrying out extensive molecular profiling and coupling driver mutations to specific selective inhibitors fostered the advent of new methodologies and trial designs. We systematically reviewed the precision oncology trials published in the last 20 years.

METHODS

We included all the precision oncology trials published between January 2000 and June 2021. We collected data about screened patients, enrolled patients, overall response rate (ORR), progression-free survival (PFS), overall survival (OS), toxicities, and quality of life (QoL).

RESULTS

In the exanimated period, 34 papers were published for 27 different trials. Most of the studies (82%) had a basket design and were non-randomized (81%) (**Table 1**).

In total, 20790 patients were screened, with an average of 990 (35 - 5548) patients per study. The average duration of the enrollment phase was approximately 32 (9-88) months. Overall, 3865 patients were enrolled (18% of screened patients), with an average of 114 (10 - 514) patients per study. An ORR was recorded in 426 patients (11% of enrolled patients, 2% of screened patients) with a mean of 12 patients per single study (**Figure 1**).

Toxicity data were included in 26 publications (76%), while none of the publications had the patient-reported quality of life data.

Table 1. Study characteristics

Type of studies	**n° (%)**
Basket trial	22 (82)
Umbrella trial	4 (15)
Platform trial	1 (3)
Randomization	
Yes	6 (19%)
No	21 (81%)
Primary endpoints	
OS	1 (3%)
PFS	3 (11%)
ORR	23 (86%)
QoL	0 (0%)

Finally, we found that 23 trials (86%) used ORR as the primary endpoint, 31 publications (91%) reported PFS data, while only 18 publications (52%) reported OS data (**Table 1**).

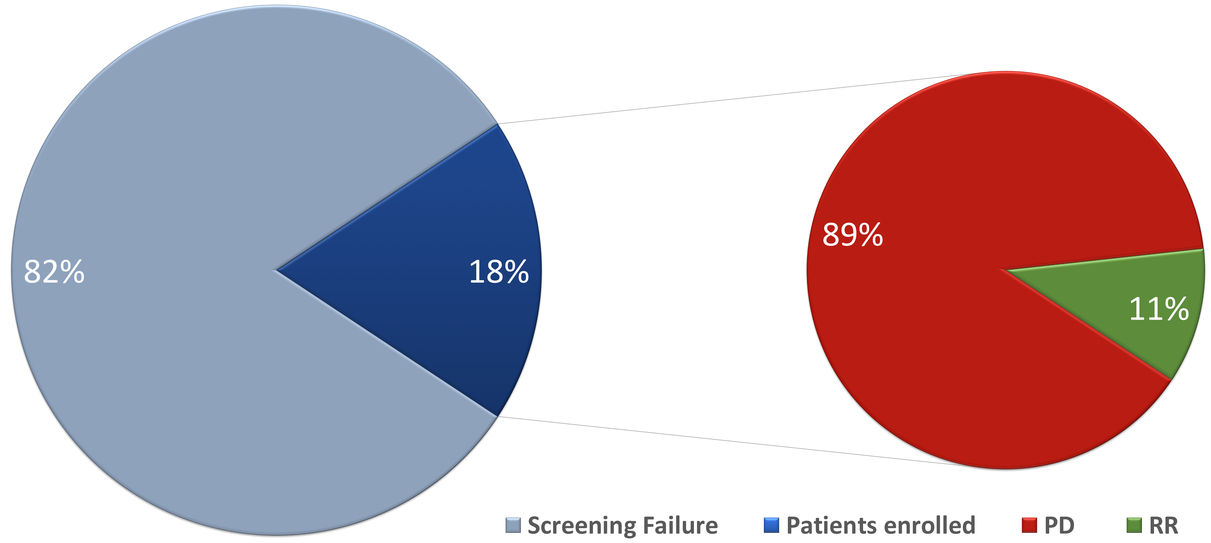

Figure 1. Patient's attrition and response rate

CONCLUSIONS

In this analysis, we intended to offer a snapshot of the results produced by precision oncology studies over the past twenty years. In total, these studies enrolled a low percentage of patients, less than 20%.

Moreover, we show that most of the trials evaluated ORR as a primary endpoint, and in about half of the publications, no data of OS was reported.

In conclusion, despite the vast effort produced in the screening phase, precision oncology trials had modest results and often reporting incomplete data regarding OS, toxicity, and QoL.

M. Filetti has no conflicts of interest to declare. Contacts: marco.filetti@guest.policlinicogemelli.it