The AVALPROFS study
Assessing the VALue of PROgression Free Survival

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Background

The goals of advanced cancer treatment are to improve quantity and/or quality of life (QoL). In this setting novel cancer drugs are increasingly being licenced on the basis of progression free survival (PFS) alone. This is contentious because although attractive for methodological and practical reasons in clinical trials, PFS is not always a surrogate for overall survival (OS). Furthermore, proof that PFS leads to improved QoL is limited since few trials include patient reported outcomes (PROs) or directly address if disease stabilisation is worth treatment side effects[1]. The value of PFS to patients therefore warrants investigation. The AVALPROFS study sets out to do this and the pilot phase is reported here.

Aims

Design a study and develop materials & methods to investigate potentially sensitive issues underlying the value of PFS to patients.

Methods

A longitudinal study design and contents of 4 semi-structured interviews were developed with a patient advisory group drawn from members of Independent Cancer Patients' Voice (ICPV). Patients receiving drugs offering only PFS or modest OS gains provided feedback about the acceptability and comprehensibility of the interviews, the inclusion of validated QoL measures (FACT and STAI) and 2 versions (see figures 1 & 2) of a tool to capture the trade-off between time a therapy controls the cancer (i.e. PFS) and a worst side effect.

Figure 1: Sliding response scale

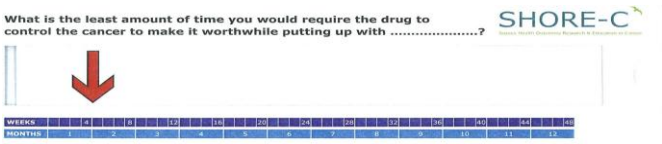
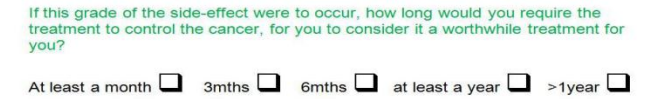


Figure 2: 5-point option response scale



The semi-structured interviews developed were:- A -pre-treatment, B -on treatment, C -at treatment cessation due to disease progression, D -at treatment cessation due to toxicity.

Interview questions developed covered:-
Section 1 - demographics
Section 2 - about current symptoms, background to treatment initiation or current therapy status, comprehension of the phrase PFS and the understanding & expectations about therapeutic aims of the treatment, perceptions & any experiences of treatment related toxicity (side effects) were recorded using a booklet & grades adapted from CTCAE manual, figure 3
Section 3 - trade-off questions determining preferences for balance between PFS time and a worst side effect

Figure 3: Example from adapted side effect booklet

Diarrhoea definition: frequent & watery bowel movements		
Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)
Increase of 4 or fewer loose/watery stools a day over what is usual for you	More than 4 but fewer than 7 loose/watery stools a day	7 or more loose/watery stools a day, could cause incontinence

Participants

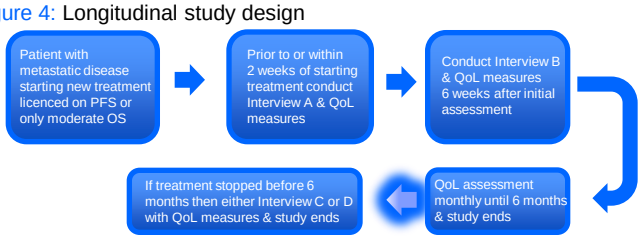
- 11/19 patients approached participated
- 4 prior to starting a novel cancer drug
- 3 on a novel cancer drug
- 4 at cessation of a novel cancer drug due to toxicity
- Age: mean =59yrs, range 40-70yrs
- Sex: 6 female, 5 male
- Treatments included: erlotinib, cetuximab, vemurafinib, gefitinib, everolimus, pertuzumab

Results

- constructive feedback permitted modification of the interview schedule questions & confirmed acceptability of the QoL measures
- some patients found the trade-off questions difficult
- a 5-point option scale was preferred for the trade-off questions
- only one patient recalled the phrase PFS used during the consultation about their new treatment
- 6/11 patients had no idea what PFS means, one saying "it sounds positive, hopeful, as it's got the word survival in it"
- all patients reported they were comprehensively warned about the possible side effects of treatment
- diarrhoea was most commonly reported as the worst side effect patients had experienced
- belief that extending life was the therapeutic aim or a benefit of the treatment was common (see table below

Beliefs about:	Treatment aims	Treatment benefits
feel better	4	4
extend life	4	4
slow cancer growth	8	9
shrink the cancer	4	
control symptoms	4	
give hope	1	2
doing something helps	2	3
reduces anxiety		2

Figure 4: Longitudinal study design



Conclusions

- collaborative working with ICPV enabled the initial design and study materials development
- patients' feedback refined the design, interviews and other tools
- the pilot work led to this potentially difficult and sensitive, but essential longitudinal study being initiated
- longitudinal study recruiting in 15 UK centres
- 64 patients to-date enrolled in the AVALPROFS study

Acknowledgements: Many thanks to patients, clinicians, ICPV advisory panel members and Boehringer-Ingelheim for an unrestricted educational grant

Reference: [1]Fallowfield & Fleissig (2011) The value of progression-free survival to patients with advanced-stage cancer. *Nature Reviews-Clinical Oncology*, 9 (1) 41-7