# Assessing the VALue of PROgression Free Survival (AVALPROFS)

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## Abstract

**Background:** Although attractive for methodological & practical reasons, progression free survival (PFS) is not always a surrogate for overall survival (OS). Few trials include relevant patient reported outcomes (PROs) or directly address if disease stabilisation is worth treatment side effects. **Methods:** A pilot study obtained feedback from patients having drugs offering only PFS or modest OS gains, about the acceptability and comprehensibility of PRO measures for use in a longitudinal study. These included validated QoL tools and 4 study specific interview schedules developed in close collaboration with Independent Cancer Patients' Voices (ICPV). **Results:** 11 pts with metastatic cancer participated. Only one recalled the phrase PFS used in clinical consultations. Few knew their latest scan results. Some were confused about the therapeutic aims of further treatment, 4 thought it would extend survival. All had experienced or anticipated considerable treatment related toxicity. Most were not upset by the interview schedules, provided comprehensive feedback about these and the trade-off questions. **Conclusions:** PFS is confusing and questions remain about its true value. Involvement of ICPV in potentially distressing research about study design, together with inclusion of feedback from pilot patients was invaluable. The longitudinal AVALPROFS study is now recruiting.

## Background

Extraordinary advances have been made in the past decade with more patients cured of cancer and/or surviving longer; but psychosocial and iatrogenic harms are created by the diagnosis, symptoms of disease and treatment side-effects. Many harms are under-recognised, under-reported & consequently undertreated. Likewise potential benefits may be underestimated as patients' treatment experiences, impact on general, social, emotional and functional well-being, are not well captured; proxy rater CTCAE assessments of toxicity (frequency & severity) differ from those of patients.[1] Increasingly, novel drugs are approved on the basis of PFS benefit alone. Quality not just quantity of life is an important consideration. The need to balance improved disease control with harms of therapy raises 2 questions - does PFS really result in discernable clinical benefit for patients and are 'benefits' worth adverse treatment related symptoms.[2]

## Aims

- to develop 4 study specific interview schedules
- gain feedback from patients about study design and to inform modification of interviews for use in the longitudinal study
- test 2 different methods for ascertaining trade-offs between time needed to control cancer growth and worst side-effects

## Background

Four draft semi-structured interview schedules were developed :-

A. pre-treatment
B. whilst on treatment
C. at diagnosis of disease progression
D. when treatment is halted due to unacceptable toxicity

Sections 1 & 2 of each schedule comprised questions covering personal details: demographics, age, education etc. and current understanding about therapeutic aims of treatment

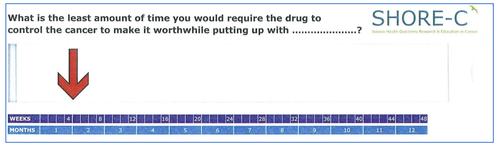
Section 3 covered:-

- understanding of progression free survival
- preferences for quality v quantity of life
- FACIT QoL questionnaires to be used in the longitudinal study
- perceptions about treatment related toxicity (side effects) using booklet & grades adapted from CTCAE manual [a]
- preferences for a sliding scale [b] or a response scale with predefined prompts/options [c] to determine trade-offs
- feelings about the questions used in the draft interviews – particularly content, clarity and acceptability

[a] example from 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 |




[b] sliding scale

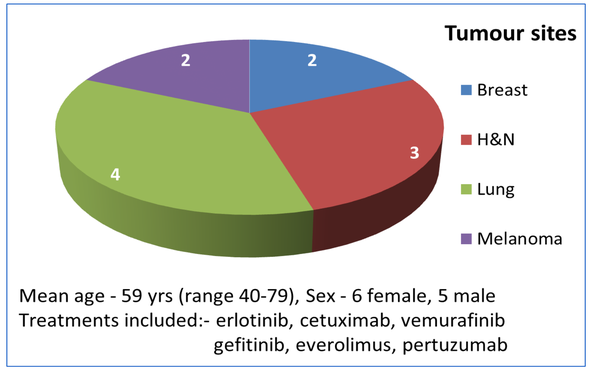
[c] response scale

If this grade of the side-effect were to occur, how long would you require the treatment to control the cancer, for you to consider it a worthwhile treatment for you?

At least a month ❑ 3mths ❑ 6mths ❑ at least a year ❑ >1year ❑

## Pilot participants

- 11/19 patients approached participated
- 4 prior to starting new treatment
- 3 on treatment
- 4 who had discontinued treatment due to toxicity




Mean age - 59 yrs (range 40-79), Sex - 6 female, 5 male

Treatments included:- erlotinib, cetuximab, vemurafinib gefitinib, everolimus, pertuzumab

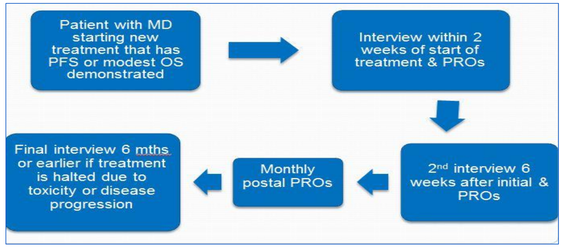
## Results

- patients gave constructive feedback about interview schedules & QoL questionnaires
- trade-off questions difficult for some, response scale [c] preferred
- only one recalled "Progression Free Survival" being used during consultation with doctors and 4 had no idea what phrase meant: *"sounds positive, hopeful to me as it's got the word survival in it"*
- all patients were warned about possible treatment side effects
- worse side effect experienced was diarrhoea

| Beliefs about:- | aims of new treatment | benefits of new tmt are / will be |
|---|---|---|
| feel better | 4 | 4 |
| extend life | 4 | 4 |
| slow the cancer | 8 | 9 |
| shrink cancer | 4 | |
| control symptoms | 4 | |
| give hope | 1 | 2 |
| doing something | 2 | 3 |
| reduce anxiety | | 2 |

## AVALPROFS longitudinal study

- pilot results shared with patient advisory group
- interview schedules and study design finalised
- patient representatives attended ethics review meetings with PI
- longitudinal study recruiting in 15 UK cancer centres




## Summary

- drugs that arrest the progression of cancer for a while may reduce tumour burden and symptoms of disease
- unless treatment related side-effects can also be identified and effectively controlled, these new treatments may not be valued by patients
- hypothetical studies looking at time trade-offs have been conducted in this area, but important contemporaneous research with patients during therapy has not
- ethics committees and others share concerns about upsetting patients with metastatic disease about actual therapeutic gains
- committed early involvement of patients in development of measures & study design, followed by piloting assists in the initiation of comprehensive longitudinal studies like AVALPROFS

## References

1. Basch E, Jia X, Heller G et al. (2006) Adverse symptom event reporting by patients vs clinicians: relationships with clinical outcomes. *Journal of National Cancer Institute*, 101(23), 1624-32
2. Fallowfield L & Fleissig A. (2011) The value of progression-free survival to patients with advanced-stage cancer. *Nature Reviews. Clinical Oncology*, 9(1) 41-7

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