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 licensed 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. 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.

Results

- 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

- 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 found the trade-off doubts about the value of PFS, but patients had experienced
- belief that extending life was the therapeutic aim or a benefit of the treatment was common (see table below)

<table>
<thead>
<tr>
<th>Beliefs about:</th>
<th>Treatment aims</th>
<th>Treatment benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>feel better</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>extend life</td>
<td>4</td>
<td>4</td>
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<tr>
<td>slow cancer growth</td>
<td>8</td>
<td>9</td>
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<tr>
<td>shrink the cancer</td>
<td>4</td>
<td></td>
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<td>control symptoms</td>
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<td>give hope</td>
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<td>2</td>
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<td>doing something helps</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>reduces anxiety</td>
<td>2</td>
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</tbody>
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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