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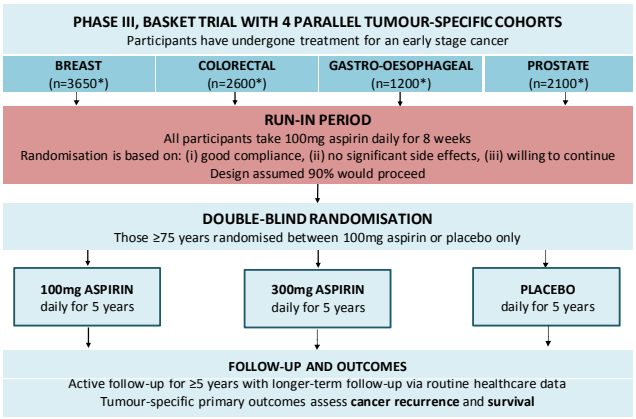
Use of an active run-in period in a cancer trial: The Add-Aspirin experience

Why use a run-in period?

- Add-Aspirin is assessing use of daily aspirin for the prevention of recurrence following cancer treatment (see schema)
- It's likely that aspirin must be taken for a number of years to see an effect. Since aspirin is available over-the-counter, non-compliance is a concern. Additionally, little is know about toxicity in this setting.
- An active run-in period was incorporated: participants take aspirin 100mg for 8 weeks prior to randomisation to assess compliance and tolerability
- The population selected for randomisation may be more compliant in the longer term with a resultant increase in power
- Here, we consider implementation of the run-in period through:
  i. Randomisation rates and other data from a 2-year feasibility phase
  ii. A survey of recruiting teams on acceptability and impact of the run-in

Trial design



* n= target randomisations; the number registered will be based on the assumption that 10% will not proceed after the run-in.

Implementing the design

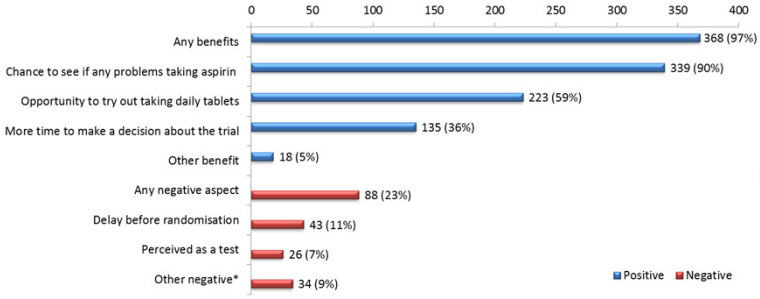
Feasibility data

- In the first 2 years, 3493 participants registered from 149 UK centres. Centres in India (11) and Republic of Ireland (11) subsequently joined.
- 85% (2719/3194 who had finished the run-in) proceeded to randomisation, and this was similar across tumour types
- Where a main reason for not continuing was given, participant choice (37%) and (minor) toxicity (32%) were the most common. Smaller numbers of participants had disease progression or were found to be ineligible. Decisions were often multi-factorial.
- Very few participants had significant toxicity (11, 0.5% CTC grade 3)
- Reported adherence was high (95% took 6-7 tablets a week)

Survey of recruiting teams

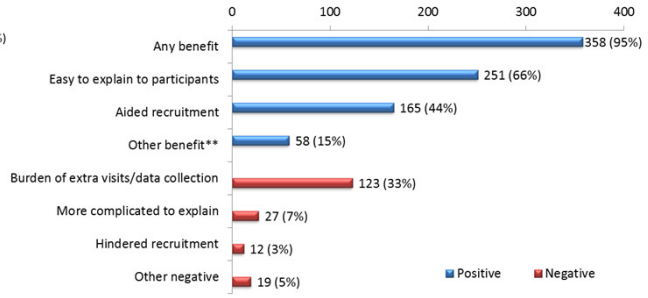
- 378 responses were received, primarily from research nurses (59%) and recruiting investigators (30%), at 153 (of 196, 78%) centres across the three countries
- Respondents felt that participants viewed the run-in positively (73%) or neutrally (27%)
- Researchers themselves generally viewed it positively (80%); only 2% viewed it negatively
- Most respondents identified benefits of the run-in for both participants (97%) and research teams (95%). Though negative aspects were also identified by some (see figures).
- Opinions were divided as to whether the run-in increased recruitment (35% felt it did, 26% felt it did not, 39% were unsure)

Positive and negative aspects of the run-in for participants



* An additional hospital visit was a negative aspect commonly reported under "other".

Positive and negative aspects of the run-in for recruiting teams



** The opportunity to assess tolerability was a benefit commonly reported under "other".

Conclusion

The run-in period is viewed positively by participants and research teams, with a number of benefits identified.

The drop-out rate (15%) suggests the run-in provides a useful screen for non-compliance and poor tolerability, and may reduce the risk of poor compliance during the randomised phase. Longer term data will be needed to demonstrate this.

Run-in data have also confirmed the feasibility and acceptability of aspirin for the majority of patients in this setting.

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