Desmoplastic Small Round Cell Tumour group
Working Group Meeting Minutes

Saturday 28th September 2013, 13.45pm – 15.45pm
Cairo/Melbourne room, The Hilton Amsterdam Airport, Schiphol

Meeting attendees:

Jeremy Whelan	Larry Hayward	Iris Pauporté
Winnette Vander-Graaf	Anna Frezza	Nicola Keat
Sandrine Marreaud	Saskia Litiere	Andrea McConnell

In Circulation:-

Ian Judson	Helen Hatcher	Matt Seymour
Bob Maki	Alessandro Gronchi	Kate Law
Doug Hawkins	Jeanne-Marie Brechot	Denis Lacombe
Fabien Calvo	Paolo Casali	Anastassia Negrouk
Tom Gross	Ted Trimble	Jack Welch

1. Aim of the meeting

Jeremy Whelan (JW) introduced the group and provided a summary of the discussion from the IRCI DSRCT meeting alongside ASCO 2013 (see attached minutes for further information). JW explained that the aim of the Working Group Meeting was to develop a trial idea that could be presented to the IRCI DSRCT group.

2. Background information

Anna Frezza (AF) presented the results of a survey that she and JW had conducted to collect information about current practice. Respondents were from Europe, USA and Australasia allowing some very cautious intercontinental comparisons (please see appendix 1). AF highlighted that between the EU and US there are similarities with regards to the need for a trial with the primary priorities of either investigating first line therapy, setting up a registry or investigating maintenance options. JW advised that the questionnaire was distributed primarily amongst US paediatric sarcoma clinicians, and that as the response from adult sarcoma specialists may be less well represented in the results.

JW recalled that at the ASCO 2013 meeting the first discussions on this topic had highlighted significant differences of opinion on the best way forward.

3. Study in the first line setting

Larry Hayward (LH) thought that it would be difficult to carry out a randomised trial in the first line setting, as it is hard to define a standard Ewing's Regimen agreeable across all groups, which would make it difficult to define the study arms and numbers needed for such a study may be excessive in view of the high response rate to first line treatment. JW highlighted that clinicians know that they want to give patients chemotherapy as they will respond, and that the different schedules are only minor variations. JW suggested that perhaps a study comparing VIDE and a less intensive chemotherapy such as VAC could be investigated to see if the same result could be achieved with less toxicity. Winnette Vander-Graaf (WVG) did not think that this would be a popular design with US clinicians, who are looking to cure rather than to reduce toxicity. The Working Group concluded that a trial of first line induction treatment was not feasible at this stage.

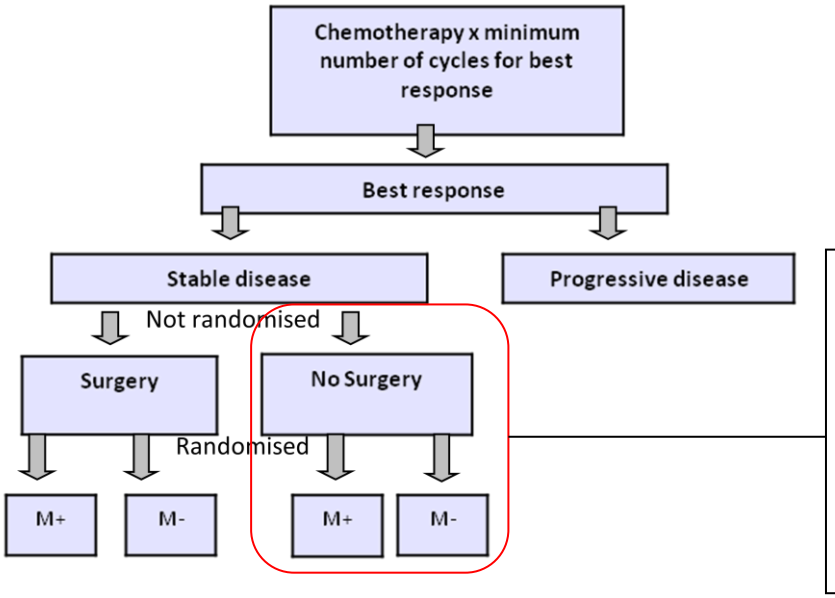
4. Maintenance question

The group discussed a scheduling question comparing early maintenance with late maintenance. A Multi-Arm, Multi-Stage (MAMS) design comparing Pazopinib, Carbozatinib, VAC and placebo was also discussed. WVG

suggested potentially approaching Novartis regarding randomising to an MTOR inhibitor. JW noted that a maintenance question would be relevant to all patients, however would present some methodological challenges in the design, particularly with regards to:-

- The *heterogeneity of residual bulk* (which is difficult to measure) between patients following first line chemotherapy. The challenge would be how to contend with the differing disease burden. Saskia Litiere (SL) noted that they would need to understand this to gauge overall survival in order to be able to work out the statistics. JW and LH highlighted that it is important to note that even thought there is heterogeneity in theory, this makes very little difference in practice, as there is still little difference in survival. Therefore OS should still be informative.
- *The varying approaches to de-bulking surgery between centres*. Some centres undertake surgery much more frequently than others due to the varying level of confidence amongst the surgeons, and the threshold for surgery varies between centres. The group questioned whether anything could be learnt from how disease burden has been managed in gynaecological randomised studies (and whether this would illuminate possibilities of addressing a question about the role of surgery).

It was proposed that patients could be given first line chemotherapy for a minimum number of cycles for best response. It was proposed that the recommended first line chemotherapy regimen could be specified as doxorubicin plus an alkylator. Best response would be measured by RECIST. Possible designs were then discussed as follows:



LH thinks that this design would be feasible if the maintenance drug was interesting enough to convince people to randomise. WVG thought that this option is also the most feasible to sell.
JW advised SL that possibly a survival improvement of 6 months would be beneficial.

JW highlighted that a clinicians decision to randomise will be dependent on the maintenance treatment, e.g. If treatment is VAC they won't mind randomising to M- as they might believe that VAC is unlikely to make a difference. However if maintenance is Pazopanib, the clinicians might think that this will be beneficial and therefore it will be more difficult to randomise to M-. It was suggested that the randomisation could be to M1 vs. M2 (i.e. between 2 different maintenance treatments if no maintenance is not considered acceptable).
M+ (Maintenance) = MAMS design with mTOR inhibitor, Carbozantinib, Pazotinib and VAC with 20 patients per arm
Primary endpoint= OS

s6.	**AOB** ***Registry;*** JW advised that following the meeting at ASCO 2013 Pooja Hingovani had agreed to work on a registry, although there was no immediate expectations for this in the near future due to her maternity leave. It was thought that a registry component should be included in the trial under development. ***Consensus statement;*** JW advised that he was due feedback from Melinda Merchant, who had agreed at the ASCO 2013 meeting to take the lead on developing a consensus statement. ***Translational research*;** the value of the study in development for tissue collection and retrospective genomic analysis was acknowledged.
7.	**Next steps/actions** **SL:** to look into the EORTC Sarcoma database for data available on patient survival. **All:** to look into whether anything can be learnt from how disease burden has been managed in gynaecological randomised studies. **All:** trial design to be further discussed at the EORTC Sarcoma meeting in Budapest [*Post meeting note: the proposal was discussed in brief at the Budapest meeting. Support was given to continue working on it].* **AF** to circulate a discussion paper developing options discussed at this meeting.