I have no important comments on the technical aspects of the Health Economic analysis, but some observations on the application in general

1. Throughout the comparison is with ASC not CAV, but I am not convinced this is appropriate. If funded then oral topotecan will become the standard second line regimen and CAV third line, despite the likely economic advantages of CAV, simply because access to topotecan will at least initially be controlled but access to CAV is not (as has happened with docetaxel and erlotinib where most patients probably now receive both, although the original SMC decision was predicated on either/or) and hence with topotecan available there will be 3 lines of therapy rather than 2 provided topotecan is given before CAV. This would imply very careful definition of those who might receive CAV and what exclusions would justify topotecan but I would still expect a dramatic increase in needle phobia which resolves nearer the end of life. I understand that the amrubicin *vs* topotecan trial is proving difficult to recruit because the comparator is d1-5 iv topotecan not oral topotecan.

2. I am not sure the missing QoL data issue is easily overcome - if only 40% of data points are available I think what is left becomes fairly meaningless because of the uncertainties involved (not all the missing data can be end of life else it implies 60% of time on trial is spent dying, not a good recommendation for the drug). Hence there must be some doubt about the assumptions regarding QALYs made in the analysis.

3. I think with these numbers subgroup analyses are impossible and should be deleted.

4. I think no wastage is unlikely, if only because patients will be admitted during chemotherapy cycles, or feel unwell at home, and will not take all their drugs. Moreover the small number of patients involved at any one centre makes it unlikely that extra drug can be divided between more than one patient. There is also the question of whether the current presentation of the drug remains the same if funded.

I think the analysis is excellent but might be compromised by the limited data, and at risk of manipulation by doctors who want to treat patients after the decision, and who will place their views about maximising patients access to therapy above economic considerations. Overall I am not impressed there is a clinical need for this drug (which is the conclusion we reached after the presentation of the CAV *vs* topotecan data in 1997), but I am sure it will be used if available, and to a greater extent than anticipated.