

PGT-A

Strategic delivery: Safe, ethical, effective treatment Consistent outcomes and support Improving standards through intelligence

Details:

Meeting	SCAAC
Agenda item	4
Paper number	SCAAC (08/06/2020) 004
Meeting date	08 June 2020
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Output:

For information or recommendation?	For recommendation
Recommendation	<p>Members are asked to:</p> <ul style="list-style-type: none"> • consider the quality of evidence for PGT-A based on the findings from an independent assessor; and in the light of that assessment • consider whether the information published on the HFEA website for PGT-A should be revised to include: <ul style="list-style-type: none"> – that there is reasonable evidence that PGT-A can reduce the chance of miscarriage, particularly in older women – that it can improve the time to pregnancy, and following that live birth rates, again in older women.
Resource implications	N/A
Implementation date	With immediate effect
Communication(s)	N/A
Organisational risk	<input checked="" type="checkbox"/> Low <input type="checkbox"/> Medium <input type="checkbox"/> High
Annexes	None

1. Background

- 1.1. The SCAAC consider the ‘traffic light’ ratings of the treatment add-ons listed on our [website](#) on an annual basis. SCAAC review the available evidence, focusing solely on [randomised controlled trials \(RCTs\)](#), and consider any changes to the traffic light rating based on this evidence and whether the particular add-on is likely to improve the live birth rate. The process is informed by recommendations made by an independent expert in systematic reviews and evidence from an independent assessment of the quality of evidence for each treatment add-on.
- 1.2. The rating for PGS on day 5 embryos was changed in [October 2019](#) from an amber to a red traffic light rating. The decision was informed by two newer studies and three RCTs previously reviewed in 2017. The studies showed no benefit to live birth rate.
- 1.3. The HFEA have received a number of detailed letters and other feedback taking issue with the decision to classify PGT-A as red. Although the comments raised do vary, there is a degree of commonality. Crucially, they argue that the exclusive focus on live birth rate in the traffic light assessment process has meant that other demonstrable benefits of PGT-A have been ignored: namely a role in shortening the time to pregnancy, and reducing the misery of repeated treatment cycle failure, or miscarriage.
- 1.4. Given the serious questions raised, the HFEA have commissioned a revised assessment from the external expert to look at findings additional to live birth rate that have been reported in the RCTs reviewed by the SCAAC. The independent assessment is attached at Annex A In addition, a summary of the concerns raised are set out in section 2 of this paper.
- 1.5. Many of the comments outlined in these communications are concerned with SCAACs traffic light review process, including the exclusive focus on RCTs. These methodological issues will be addressed in the broader policy work we have planned on treatment add-ons.

2. Summary of concerns raised

- 2.1. The comments we have received about PGT-A are supportive of several aspects of the position that SCAAC has reached. There is recognition that PGT-A on 3 day embryos is appropriately rated red. There is agreement that even on 5 day embryos PGT-A cannot improve the quality of a particular embryo and none of the comments we have received suggest that there is reliable evidence that it can improve live birth rate per cycle started.
- 2.2. The criticism focuses principally on the failure to consider outcomes other than the impact on live birth rate and the terminology that is used to define an add-on as ‘red’. A useful summary of this position can be found in an article in a recent ARCS newsletter. The relevant extract reads: ‘The awarding of “two red lights” for the use of PGT-A some might say is justified based on the fact that the RCTs are not unequivocal. To say there is “no evidence” to support the use of PGT-A is, however, quite simply, factually incorrect. Shame on you HFEA, there are pages and pages of evidence. If they don’t yet meet the standards that you have set, then say so. But please don’t confuse patients further with statements that have no basis in fact, and please don’t lump PGT-A alongside endometrial scratch and homeopathy’
- 2.3. Critics point out that while there may be reasonable evidence that PGT-A may not improve live birth rate, there is some evidence that its use is associated with a considerable reduction in the

chance of miscarriage, particularly in older patients. As noted above, the SCAACs review of traffic light ratings is based on live birth rate.

- 2.4.** Some recognised that more robust clinical trials are required to prove conclusively whether PGT-A is effective in improving treatment outcomes; and for whom. Whilst others strongly contested that the only way to be confident that a treatment is routinely effective in treatment is on the basis of evidence from an RCT.
 - 2.5.** The comments were in agreement that there are many challenges in the conduct of RCTs and requiring this level of proof places a barrier to the use of treatments where other data may exist to support their use. It is frequently raised that often an RCT is either not appropriate or feasible, therefore that evidence needs to be gleaned from other valid statistical methods.
 - 2.6.** Many regard the non-selection studies as more relevant and powerful than RCTs: in that they provide strong evidence of:
 - a) the existence of aneuploid embryos and
 - b) their failure to produce healthy live births; in distinct contrast to
 - c) euploid embryos that produce live births at a rate of ~60% - or higher - in the best clinics.
 - 2.7.** We have been informed that the decision to classify PGT-A as red is starting to impact on clinic and patient behaviours: some clinics are now suggesting to patients that they should ignore the traffic light ratings because of it; and some patients are apparently so confused that they have requested that their aneuploid embryos be replaced. This poses a reputational risk to the traffic light system.
 - 2.8.** In addition, it was argued that some practitioners may feel uncomfortable about not offering a technique to detect the prevalence of aneuploidy in human embryos which has a high degree of accuracy. There was concern in the correspondence that should a child be born with an aneuploid condition or a miscarriage occur then this might prompt litigation for negligence in not having raised the benefit of PGT-A, if it were deemed that during IVF practice the use of PGT-A could have avoided this. Whether any such litigation would be successful is not known.
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3. Conclusions

- 3.1.** Many of those in the sector consider the benefits of PGT-A extend beyond increasing live birth rates, by helping patients understand and accept the reasons why treatment cycles may have failed, and to make decisions about their future options. They also believe that PGT-A has a role in shortening the time to pregnancy, and reducing repeated treatment cycle failure, or miscarriage.
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4. Recommendations

- 4.1.** Members are asked to
 - consider the quality of evidence for PGT-A based on the findings from an independent assessor; and in the light of that assessment
 - consider whether the information published on the HFEA website for PGT-A should be revised to include:

- that there is reasonable evidence that PGT-A can reduce the chance of miscarriage, particularly in older women
- that it can improve the time to pregnancy, and following that live birth rates, again in older women.