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## Formalised consensus of the European Organisation for Treatment of Trophoblastic Diseases on management of gestational trophoblastic diseases

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### KEYWORDS

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**Abstract** Gestational trophoblastic disease (GTD) is a spectrum of cellular proliferations arising from trophoblast. Their invasive and metastatic potential sometimes requires chemotherapy and/or surgery. Current management is generally associated with favourable prognosis. Therefore, treatments must be chosen according to the desire for further childbearing of each patient. The European Organisation for Treatment of Trophoblastic Diseases (EOTTD) is dedicated to optimise diagnosis, treatment, follow-up and research in GTD by bringing together knowledge of clinicians and researchers from 29 countries working in the field of GTD in Europe. This study assessed the level of agreement among an expert panel of the EOTTD in order to rationalise the management of patients in Europe. The RAND/UCLA Appropriateness Method was used to combine the best available scientific

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trophoblastic tumour  
Epithelioid trophoblastic  
tumour

evidence with the collective judgment of experts to yield a statement regarding the appropriateness of performing a procedure at the level of patient-specific symptoms, medical history and test results. There was an agreement for 54 statements while the experts showed a disagreement for two statements. As there is little evidence from randomised trials on which to base recommendations about management of GTD, many of these recommendations are based on expert opinion derived from changes in management fact that have improved outcomes from nearly 100% fatality to nearly 100% cure rates. However, a large agreement among experts is invaluable to the individual clinician who is struggling to decide whether a fertility-sparing treatment of hydatidiform mole or a low-risk GTN can be chosen and how it must be conducted.

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## 1. Introduction

Gestational trophoblastic disease (GTD) is a spectrum of cellular proliferations arising from the different types of trophoblast encompassing five main clinicopathologic forms: hydatidiform mole (complete and partial), invasive mole (IM), choriocarcinoma (CC), placental site trophoblastic tumour (PSTT) and epithelioid trophoblastic tumour [1,2]. These diseases are predominantly found in women of reproductive age from all ethnic groups and their invasive and metastatic potential sometimes requires chemotherapy and/or surgery. Current management is generally associated with favourable prognosis. Therefore, treatments must be chosen according to the desire for further childbearing of each patient.

The European Organisation for Treatment of Trophoblastic Diseases (EOTTD) is dedicated to optimise diagnosis, treatment, follow-up and research in GTD by bringing together knowledge of clinicians and researchers from 29 countries working in the field of GTD in Europe. European countries included in the EOTTD have much in common, of which the incidence of gestational trophoblastic diseases, general health care system organisation, and availability of medical and paramedical examinations. The following recommendations have been established by an expert panel of the EOTTD in order to rationalise the management of patients in Europe. Randomised clinical trials comparing treatment or follow-up strategies are generally either not available or cannot provide evidence at a level of detail sufficient to apply to the wide range of patients seen in everyday clinical practice. Therefore, the RAND/UCLA Appropriateness Method (RAM) was used to combine the best available scientific evidence with the collective judgment of experts to yield a statement regarding the appropriateness of performing a procedure at the level of patient-specific symptoms, medical history and test results.

Forty-five experts from 16 countries of EOTTD were asked to rate 56 statements twice according to how appropriate they felt each statement was in properly managing patients with GTD.

## 2. Material and methods

According to the RAM [3], an 8-member steering group of the EOTTD critically reviewed the literature to summarise the scientific evidence available on GTD management and developed a list of 56 statements to be rated by an expert panel. The main selection criteria for the constitution of the expert panel were acknowledged leadership in the field of GTD, absence of conflicts of interest, geographic diversity and a multidisciplinary practice setting. Forty-five experts from 16 countries of EOTTD were selected and sent the list of statements along with the literature review and instructions (Table 1). The experts were asked to rate each statement using a 7-point scale according to how appropriate they felt each statement was in properly managing patients with GTD. A score of 1 indicates that the statement is highly inappropriate and 7 that it is highly appropriate. The experts rated each of the statements twice, in a two-round ‘modified Delphi’ process [4]. In the first round, the ratings were made individually at home, with no interaction among experts. In the second round, the experts met face-to-face for 1 day under the leadership of a moderator, discussed the rating focusing on the areas of disagreement, modified the original list of statements if needed and rerated each statement individually.

The definition of agreement and disagreement among experts was defined according to the number of experts rating each statement [4] (Table 2). Agreement was defined by a number of experts rating outside the region containing the median value (1–2, 3–5, 6–7) of  $\leq 12$ ,  $\leq 13$  and  $\leq 13$  for a total number of experts of 39, 41 and 42, respectively. Disagreement was defined by a number of experts rating in each extreme (1–2 and 6–7) of  $\geq 13$ ,  $\geq 14$  and  $\geq 14$  for a total number of experts of 39, 41 and 42, respectively.

## 3. Results

Each of the 45 experts responded to the first questionnaire and 42 out of 45 participated in the second (93% response rate). Finally, 17 statements were rated by 42

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