|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***OHSS Screening*** | **Early OHSS** | | |  | **Late OHSS** | | |  |
| ***Kisspeptin dosing group*** | **Single** | **Double** | **All** | **AD**  **(CI)**  **P value** | **Single** | **Double** | **All** | **AD**  **(CI)**  **P value** |
| ***Number of patients diagnosed with OHSS* ¥** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Normal** | 30  (96·8%) | 31  (100%) | 61  (98·4%) |  | 31  (100%) | 30  (96·8%) | 61  (98·4%) |  |
| **Mild** | 0 | 0 | 0 |  | 0 | 1 (3·2%) | 1 (1·6%) |  |
| **Moderate** | 1 (3·2%) | 0 | 1 (1·6%) |  | 0 | 0 | 0 |  |
| **Severe** | 0 | 0 | 0 |  | 0 | 0 | 0 |  |
| **Critical** | 0 | 0 | 0 |  | 0 | 0 | 0 |  |
| ***OHSS Symptoms*** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Number of patients screened by OHSS symptoms (%)** | 31  (100%) | 31  (100%) | 62  (100%) |  | 31  (100%) | 31  (100%) | 62  (100%) |  |
| **Number of patients with**  **≥1 symptom potentially consistent with OHSS (%)** | 9  (29·0%) | 7  (22·6%) | 16  (25·8%) |  | 9  (29·0%) | 9 (29·0%) | 18 (29·0%) |  |
| **Number of patients requiring medical intervention for OHSS (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients requiring hospitalization for OHSS (%)** | 1  (3·2%) | 0  (0·0%) | 1  (1·6%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| ***Sonographic Screening*** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Number of patients screened with pelvic ultrasound (%)** | 31 (100%) | 30 (96·8%) | 61  (98·4%) |  | 30 (96·8%) | 31 (100%) | 61 (98·4%) |  |
| **Mean ovarian volume in mls (SD)** | 68·6 (52·1) | 48·2 (28·9) | 58·6 (43·2) | -20·4  (-39·3, -1·5)  P = 0·034 | 28·9 (40·9) | 16·1 (15·9) | 22·4  (31·3) | -12·8  (-22·5, -3·3)  P = 0·006 |
| **Mean ovarian diameter in mm (SD)** | 41·5 (10·1) | 38·7 (7·9) | 40·2  (9·1) |  | 29·6  (9·9) | 25·9 (6·0) | 27·8  (8·3) |  |
| **Maximal ovarian diameter in mm (SD)** | 64·2 (15·1) | 58·1 (11·0) | 61·3 (13·6) | -6·1  (-12·9, 0·60)  P = 0·079 | 44·7 (14·0) | 42·4 (9·5) | 43·5  (11·9) | -2·3  (-7·7, 3·1)  P = 0·410 |
| **Number of patients with maximum ovarian diameter ≥5cm (%)** | 24 (77·4%) | 22 (73·3%) | 46 (75·4%) |  | 7  (23·3%) | 7 (22·6%) | 14  (23·0%) |  |
| **Number of patients with maximum ovarian diameter ≥8cm (%)** | 5  (16·1%) | 1  (3·3%) | 6  (9·8%) |  | 1  (3·3%) | 0  (0·0%) | 1  (1·6%) |  |
| **Number of patients with maximum ovarian diameter ≥12cm (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Total free fluid in abdomen, POD / Adnexa in mls (SD)** | 5·8 (8·1) | 3·4  (5·8) | 4·6  (7·1) |  | 3·0 (11·8) | 0·8 (2·3) | 1·9  (8·4) |  |
| **Number of patients with ≥grade 2 ascites (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients with pleural effusion (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
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| ***Blood parameters*** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| **Number of patients screened with Blood analysis (%)** | 31 (100%) | 29  (93·5%) | 60  (96·8%) |  | 30 (96·8%) | 31 (100%) | 61 (98·4%) |  |
| **Number of patients with Hematocrit >45% (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients with serum sodium ≥132mmol/L (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients with serum potassium ≥5.0mmol/L (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients with ALT ≥2xULN (%)** | 3 (9·7%) | 1 (3·4%) | 4  (6·7%) |  | 1  (3·3%) | 1  (3·2%) | 2  (3·4%) |  |
| **Number of patients with AST ≥2xULN (%)** | 2 (6·5%) | 1  (3·4%) | 3  (5·0%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patients with total protein ≥80 g/L (%)** | 1 (3·2%) | 0  (0·0%) | 1  (1·7%) |  | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  |
| **Number of patient with creatinine ≥110 µmol/L (%)** | 0  (0·0%) | 0  (0·0%) | 0  (0·0%) |  | 1  (3·3%) | 0  (0·0%) | 1  (1·6%) |  |
|  |  |  |  |  |  |  |  |  |

**Supplementary Table 2: Ovarian Hyperstimulation Syndrome (OHSS) in high risk women following kisspeptin-54 trigger**

AD = Absolute Difference (CI = Confidence Interval). Mean (SD) is presented for continuous variables and number of patients (%) for categorical variables.

¥ Diagnosis of OHSS was performed by two experienced IVF physicians (R.S., S.L.) independent of the study team provided with blinded data according to the criteria of Golan et al. 1989 with updated categorization of severe and critical OHSS by Navot et al. 1992.

POD, Pouch of Douglas; ALT, Alanine transaminase; AST, Aspartate transaminase; ULN, Upper Limit of Normal.