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| **Supplementary Table 1. Summary of the characteristics of the included studies** | | | | | | | | | |
| **Author and year** | **Study design, country, and timing** | **Sample size** | **Inclusion criteria** | **Exclusion criteria** | **Dose** | **Duration of treatment** | **Duration of follow-up** | **Outcomes** | **Results** |
| Horne et. al. 2023 | RCT, United Kingdom, between Nov 2, 2016, and  Oct 6, 2021. | 165 participants in the methotrexate plus gefitinib group and 163 in the methotrexate plus placebo group. | Women aged 1850 years, with pretreatment serum hCG levels between 1000–5000 IU/L, clinically stable, hemoglobin 100–165 g/L, and either a definite or probable diagnosis of tubal ectopic pregnancy. | Pregnancy of unknown location, intrauterine pregnancy, ectopic gestational sac >3.5 cm, intra-abdominal bleeding, abnormal liver/renal/hematologic parameters, existing lung, dermatologic, or gastrointestinal disease, and Japanese ethnicity. | Daily oral gefitinib 250 mg for 7 days, combined with a single dose of intramuscular methotrexate 50 mg/m² on Day 1. | 7 days. | 3 months. | Surgical intervention, need for additional methotrexate doses, time to resolution of ectopic pregnancy, treatment-related hospital visits, adverse events, return to menses, and treatment acceptability. | Gefitinib combined with methotrexate offered no clinical benefit over methotrexate alone for tubal ectopic pregnancy and was linked to a higher frequency of minor adverse effects. |
| Skubisz et. al. 2018 | Single-arm clinical trial with contemporaneous control, Australia and the United Kingdom, between January 2012 and April 2014. | 28 participants in the methotrexate plus gefitinib group and 32 in the methotrexate-only group. | Women aged 18-45 years, serum hCG levels at presentation between 1000–10,000 IU/L, a definite or probable diagnosis of ectopic pregnancy, and hemodynamic stability. | Japanese ethnicity, pregnancy of unknown location, intra-abdominal bleeding, prior history of lung disease, abnormal renal, hepatic, or hematologic indices, or the presence of gastrointestinal or dermatological conditions. | One intramuscular injection of methotrexate (50 mg/m²) combined with daily oral gefitinib 250 mg for seven days. | 7 days. | 6 months. | Resolution of tubal ectopic pregnancy, safety profile, tolerability, and adverse effects. | The methotrexate-gefitinib regimen achieved resolution in at least 70% of ectopic pregnancies. |
| Skubisz et. al. 2013 | Single-arm clinical trial with historical controls, conducted in Australia and the United Kingdom between October 2010 and October 2011. | Twelve participants received methotrexate plus gefitinib, while 71 were treated with methotrexate alone. | Hemodynamically stable women with serum hCG levels below 3000 IU/L, gestational sac <4 cm without fetal cardiac activity, and normal hepatic, renal, and hematologic parameters. | Japanese ethnicity or the presence of significant pulmonary, gastrointestinal, or dermatological disease. | Single intramuscular injection of methotrexate (50 mg/m²) on day 1 combined with daily oral gefitinib (250 mg). The first three participants received gefitinib for 1 day, the next three for 3 days, and the remaining six for 7 days. | The first three participants received gefitinib for 1 day, the next three participants for 3 days, and the last six participants for 7 days. | 6 months. | Safety and tolerability. | Methotrexate combined with gefitinib appeared more effective than methotrexate alone for ectopic pregnancy, though it was associated with mild adverse effects. |
| Horne et. al. 2014 | Case series from the United Kingdom and Australia. | Eight patients received gefitinib and methotrexate. | Hemodynamically stable women with non-tubal ectopic pregnancy and normal hematologic, renal, and hepatic indices. | Severe dermatological, gastrointestinal, or pulmonary disease; allergy to gefitinib and/or methotrexate; and Japanese ethnicity. | Daily oral gefitinib 250 mg for 7 days, in addition to a single intramuscular dose of methotrexate (50 mg/m²) on Day 1. | 7 days. | Ranged from 25 to 196 days. | Time to resolution,  safety,  tolerability, and adverse events. | Combination therapy with gefitinib and methotrexate showed encouraging results for women with non-tubal ectopic pregnancy. |
| Italiano et. al. 2019 | Case report and case series, Australia. | 1 received gefitinib and methotrexate, and 46 received methotrexate. | The reported case involved a live, non-tubal ectopic pregnancy in a woman with a poor surgical prognosis and high baseline serum hCG, managed medically. | NR. | Intramuscular methotrexate (1 mg/kg) is administered every other day, alternating with folinic acid 7.5 mg. Oral gefitinib 250 mg daily was initiated two days after the first methotrexate dose and continued for 7 days. | 7 days. | 1 month. | Successful resolution and occurrence of adverse events. | Gefitinib combined with multidose methotrexate appeared to be a safe and effective medical option for managing non-tubal ectopic pregnancy in this context. |
| RCT: Randomized clinical trial. GI: Gastrointestinal. HCG: Human chorionic gonadotropin. IU: International unit. NR: Not available. | | | | | | | | | |