LIPIODOL® ULTRA FLUID

Ethyl ester of iodized fatty acids of poppy seed oil

Tubal Flushing for Infertility

Fertility Enhancement: Key Studies

Effectiveness on fertility outcome of tubal flushing with different contrast media: systematic review and network meta-analysis

Ultrasound Obstetric Gynecology. Wang R et al. 2019

Oil-based or water-based contrast for hysterosalpingography in infertile women

The New England Journal of Medicine. Dreyer K et al. 2017

The FLUSH trial - Flushing with Lipiodol® for unexplained (and endometriosis-related) subfertility by hysterosalpingography: a randomized trial

Human Reproduction. Johnson NP et al. 2004
Human Reproduction. Johnson NP et al. 2007

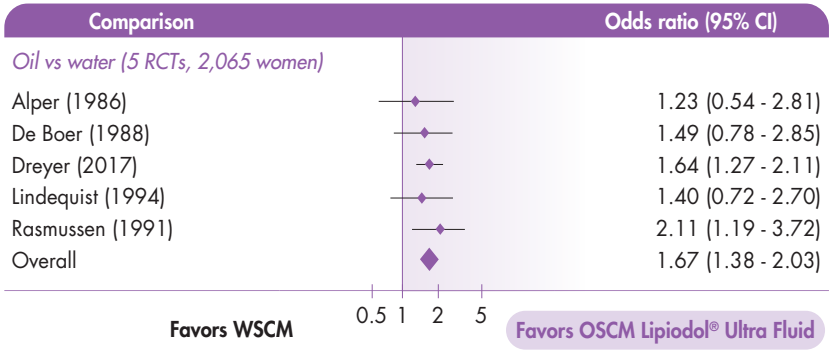
Guerbet

Effectiveness on fertility outcome of tubal flushing with different contrast media: systematic review and network meta-analysis

Ultrasound Obstetric Gynecology. Wang R *et al.* 2019

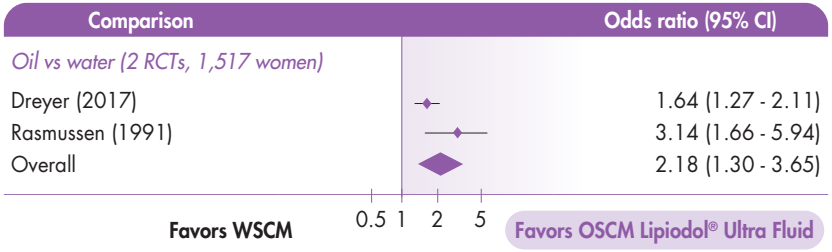
Objective: To compare, in women with infertility, the effectiveness of tubal flushing using Oil-Soluble Contrast Medium (OSCM Lipiodol® Ultra Fluid) or Water-Soluble Contrast Medium (WSCM)

Clinical pregnancy within 6 months after randomization



Read the full study

Live birth resulting from pregnancy within 6 months after randomization



Conclusion

«…In women with infertility undergoing fertility workup, ***tubal flushing using oil-based contrast medium probably increases clinical pregnancy rates within 6 months after randomization*** *and* ***may increase subsequent live-birth rates****, compared with tubal flushing using water-based contrast medium and compared with no intervention…»*

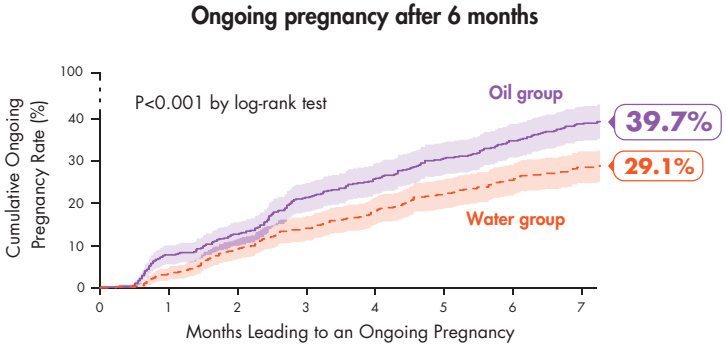
Oil-based or water-based contrast for hysterosalpingography in infertile women

The New England Journal of Medicine. Dreyer K *et al.* 2017

Objective: Evaluate the fertility enhancing effect of HSG with Oil-Soluble Contrast Medium (OSCM Lipiodol®) as compared to Water-Soluble Contrast Medium (WSCM Telebrix® Hystero)

- Multicenter randomized controlled trial
- 1,108 infertile women randomized to HSG with OSCM (n=554) or WSCM (n=554)

Results within 6 months after randomization



Read the full study

	Oil Group (n=554)	Water Group (n=554)	Rate Ratio (95% CI)	P value
Ongoing pregnancy - no. (%)	220 (39.7%)	161 (29.1%)	**1.37 (1.16 - 1.61)**	**<0.001**
Live birth ≥24 week of gestation - no./total no. (%)	214/552 (38.8%)	155/552 (28.1%)	**1.38 (1.17 - 1.64)**	**<0.001**
Miscarriage - no. (%)	29 (5.2%)	31 (5.6%)	0.94 (0.57 - 1.53)	0.79
Ectopic pregnancy - no. (%)	2 (0.4%)	2 (0.4%)	1.00 (0.14 - 7.07)	1.00
Stillbirth - no./total no. (%)	4/552 (0.7%)	4/552 (0.7%)	1.00 (0.25 - 3.98)	1.00
Median pain score on visual-analogue scale	4.8 (3.0 - 6.4)	5.0 (3.0 - 6.7)		0.28

Conclusion

*« …**Rates of ongoing pregnancy and live births were higher** among women who underwent **hysterosalpingography with oil contrast** than among women who underwent this procedure with water contrast…»*

The FLUSH trial – Flushing with Lipiodol® for unexplained (and endometriosis-related) subfertility by hysterosalpingography: a randomized trial

Human Reproduction. Johnson NP *et al.* 2004
Human Reproduction. Johnson NP *et al.* 2007

Objective: Ascertain the effectiveness of Lipiodol® flushing for enhancing fertility

- Single centre, open parallel randomized controlled trial
- 158 women randomized to HSG with Lipiodol® Ultra Fluid or to no intervention, stratified into 2 populations: 96 women without confirmed endometriosis and 62 women with endometriosis who had normal Fallopian tubes and ovaries

Results within 6 months after randomization

Live birth

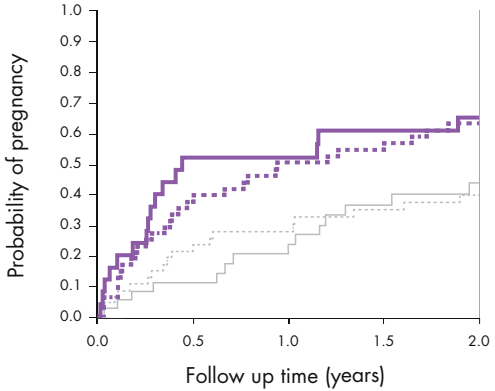
	Lipiodol® Ultra Fluid	No intervention	Relative risk (95% CI)	P value
Total population - no./total no.	23/73	11/85	**2.43 (1.27 - 4.65)**	**0.005**
Endometriosis - no./total no.	10/25	4/37	**3.70 (1.30 - 10.50)**	**0.007**
Unexplained infertility - no./total no.	13/48	7/48	1.86 (0.81 - 4.25)	0.132

Read the full studies Results at 6 months | Results at 2 years

Results 24 months after randomization

Survival curve of pregnancy over 24 months

- Lipiodol® Ultra Fluid/endometriosis
- Lipiodol® Ultra Fluid/unexplained infertility
- No Lipiodol® Ultra Fluid/endometriosis
- No Lipiodol® Ultra Fluid/unexplained infertility



Live birth plus ongoing pregnancy

	Lipiodol® Ultra Fluid	No intervention	Relative risk (95% CI)	P value
Total population - no./total no.	37/73	27/85	**1.6 (1.1 - 2.4)**	**0.02**
Endometriosis - no./total no.	12/25	12/37	1.5 (0.8 - 2.8)	0.21
Unexplained infertility - no./total no.	25/48	15/48	**1.7 (1.0 - 2.8)**	**0.05**

Conclusion

*«…Lipiodol® flushing is **effective at enhancing fertility not only for women with endometriosis, but also for those with pure unexplained infertility**…»*

LIPIODOL ULTRA-FLUID. Composition: Ethyl esters of iodized fatty acids of poppy seed oil 10 mL, corresponding to an iodine content of 480 mg/mL. **Indications (**):** For diagnostic radiology - Lymphography - Hysterosalpingography - Sialography - Ascending urethrography – Fistulography and exploration of abscesses - Exploration of frontal sinuses - Pre and post-operative cholangiography. For interventional radiology - Visualisation and localization (by selective intra-arterial use during CT) of liver lesions in adults with known or suspected hepatocellular carcinoma - Visualisation, localisation and vectorisation during Trans-Arterial Chemo-Embolisation (TACE) of hepatocellular carcinoma at intermediate stage, in adults - Visualisation and localisation of hepatocellular carcinoma at intermediate stage in adults - Selective embolization in combination with Histoacryl glue (particularly for arteriovenous malformation or aneurysms) - Selective injections of LIPIODOL ULTRA-FLUID into the hepatic artery for diagnostic purposes where a spiral CT scan is not practical. In endocrinology - Prevention of severe cases of iodine deficiency. This treatment should only be used when other methods of supplementation, particularly iodization of salt and/or drinking water, cannot be undertaken. **Posology and method of administration (*) (**):** have to be adapted according to the type of examination, the territories explored, the age and weight of the patient. The volume to be administered depends on the particular requirements of the technique and the size of the patient. Lipiodol Ultra Fluid must be administered by slow injection or via a catheter, using a suitable glass syringe or other administration devices proven to be compatible with Lipiodol Ultra Fluid. The instructions for use of these devices must be followed. **Contraindications:** Hypersensitivity to LIPIODOL ULTRA-FLUID - Manifest hyperthyroidism - Patients with traumatic injuries, recent hemorrhage or bleeding – Hysterosalpingography during pregnancy or acute pelvic inflammation – Bronchography. Interventional radiology: Intra-arterial administration of chemotherapy / Lipiodol Ultra-fluid mixture for treatment of hepatocellular carcinoma may lead to both ischemic and toxic effects to the bile ducts. Therefore, the treatment is contraindicated in areas of the liver where the bile ducts are dilated, unless post-procedural drainage can be performed. **Special warnings and precautions for use (*):** There is a risk of hypersensitivity regardless of the dose administered. Lymphography: Pulmonary embolism may occur immediately or after few hours to days from inadvertent systemic vascular injection or intravasation of LIPIODOL ULTRA-FLUID: Perform radiological monitoring during LIPIODOL ULTRA-FLUID injection and avoid use in patients with severely impaired lung function, cardiorespiratory failure or right-sided cardiac overload. Hypersensitivity: all iodinated contrast agents can lead to minor or major hypersensitivity reactions, which can be life-threatening. These hypersensitivity reactions are of an allergic nature (known as anaphylactic reactions if they are serious) or a non-allergic nature. They can be immediate (occurring within 60 min) or delayed (not occurring until up to 7 days later). Anaphylactic reactions are immediate and can be fatal. They are dose-independent, can occur right from the first administration of the product, and are often unpredictable: avoid use in patients with a history of sensitivity to other iodinated contrast agents, bronchial asthma or allergic disorders because of an increased risk of a hypersensitivity reaction to LIPIODOL ULTRA-FLUID. Thyroid dysfunction: can cause hyperthyroidism in predisposed patients. Lymphography saturates the thyroid with iodine for several months and thyroid exploration should be performed before radiological examination. Visualisation / localisation / chemoembolisation of liver tumours: Trans-Arterial Chemo-Embolization is not recommended in patients with decompensated liver cirrhosis (Child-Pugh ≥8), advanced liver dysfunction, macroscopic portal vein invasion and/or extra-hepatic spread of the tumour. Renal insufficiency must be prevented by correct rehydration before and after the procedure. Oesophageal varices must be carefully monitored. Hepatic intra-arterial treatment can progressively cause an irreversible liver insufficiency in patients with serious liver malfunction and/or undergoing close multiple sessions. The risk of superinfection in the treated area is normally prevented by administration of antibiotics. Embolization with glue: An early polymerisation reaction may exceptionally occur between LIPIODOL ULTRA-FLUID and certain surgical glues, or even certain batches of glue. Before using new batches of LIPIODOL ULTRA-FLUID or surgical glue, the compatibility of LIPIODOL ULTRA-FLUID and the glue must be tested in vitro. Indications for the use of Lipiodol Ultra-Fluid must be carefully assessed in patients with primary lymph oedema, as the oedema can be exacerbated. **Interaction with other medicinal products and other forms of interaction (*):** Metformin, Beta blockers, vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, Diuretics, Interleukin II. **Fertility, pregnancy and lactation (*):** LIPIODOL ULTRA-FLUID must only be used in pregnant women if absolutely necessary and under strict medical supervision. Breastfeeding should be discontinued if LIPIODOL ULTRA-FLUID must be used **- Effects on ability to drive and use machines:** The effects on ability to drive and to use machines have not been investigated **- Undesirable effects (*):** Most adverse effects are dose-related and dosage should therefore be kept as low as possible: hypersensitivity, anaphylactic reaction, anaphylactoid reaction, hypothyroidism, hyperthyroidism, thyroiditis, cerebral embolism, hepatic encephalopathy [a], retinal vein thrombosis, lymphoedema aggravation, pulmonary embolism, dyspnea, cough, pulmonary oedema [a], pleural effusion [a], acute respiratory distress syndrome [a], pneumonitis [a], vomiting, diarrhea, nausea, pancreatitis [a], ascites [a], hepatic vein thrombosis, cholecystitis [a], biloma [a], hepatic failure [a], hepatic infarction [a], granuloma, fever, pain, liver abscess [a], skin necrosis [a]. **Overdose (*):** The total dose of LIPIODOL ULTRA-FLUID administered must not exceed 20 mL **- Pharmacodynamic properties (*):** Pharmacotherapeutic group: X-ray contrast media, iodinated; ATC code: V08A D01.

Water-insoluble iodinated contrast medium. **Presentation (**)**: 10 mL glass ampoule. **Marketing authorization holder (*)**: Guerbet - BP 57400 - F-95943 Roissy CdG cedex - FRANCE. Information: tel: 33 (0) 1 45 91 50 00. Revision: June 13th, 2019.

(a) in the context of TAE or TACE.

(*) For complete information please refer to the local Summary of Product Characteristics (SPC).

(**) These information are intended for an international audience or are provided during an international event. Be aware that indications, posology and presentations may differ from country to country.

Reporting of suspected adverse reactions is important as it helps to continuously assess the benefit-risk balance. Therefore, Guerbet encourages you to report any adverse reactions to your health authorities or to our local Guerbet representative.

Countries in which HSG indication is registered: USA, Canada, Argentina, UK, Ireland, The Netherlands, Denmark, Turkey, South-Africa, Japan, Taiwan, Thailand, Australia & New Zealand.

For a copy of the SPC, please contact a member of Guerbet.

Not intended for US Healthcare Professionals.

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