Progestosterone plays a pivotal role in establishing and maintaining pregnancy in the bitch and in the queen. It permits the maturation of uterine cells so as to prepare them for implantation, it stimulates the glandular secretions of the endometrium required for embryo development, it closes the cervix and it reduces uterine contractility.

Anti-progestins are synthetic steroids which bind with a great affinity to progesterone receptors, preventing progesterone from exerting its biological effects. They act as true receptors antagonists, preventing the uterine effects of progesterone without initially decreasing serum progesterone concentrations. The affinity of aglepristone for uterine receptors is 3 times greater than that of progesterone itself (nine times in the queen). Progesterone concentrations after treatment only decline within 8 to 34 days to less than 3 nmol.L, due to a possible premature luteolysis caused by an increase in endogeneous PGF2α.

The anti-progestins compounds that have been tested in small animal reproduction are mifepristone (RU 486) and aglepristone (RU 534). Aglepristone (Alizine®) is the only drug available in many countries for veterinary use.

1. Use of antiprogestins in bitches.

1.1. Pregnancy termination.
Aglepristone 10 mg/kg sc given twice, 24 h apart, is the recommended dose. Aglepristone can be used from the 1st to the 45th day of mating. Antibiotics are not required when performing the treatment, unless there is a specific need to treat a known infection.

It seems preferable, to avoid failures due to a premature treatment, to wait until the end of heats to use the protocol described above. When the treatment is performed very early after mating, while the bitch is still in heat, it may be recommended to assay progesterone plasma level in order to see if aglepristone has a chance to be effective at this early stage. If the bitch has not ovulated yet, it is better to wait a few days to begin the aborting protocol (the efficacy of aglepristone after one injection is around 7 days).

Treatment before 25 days after mating result in nearly 100% in utero embryonic resorption, with generally no clinical signs observed.

Treatments after 25 days (“mid-abortion”) may lead to induced abortion within 7 days, with a prolonged vaginal discharge, mammary development and maternal behaviour patterns. This may cause inconvenience to the animal’s owner, as well as raise ethical concerns. The effectiveness of aglepristone induced abortion after 25 days is approximately 95%. In case of such a mid-pregnancy abortion, it is recommended to
perform an ultrasound examination 10 days later to ensure that a complete abortion occurred and that the uterus is empty.

After 35 days of pregnancy, it may be necessary to use a combination of aglepristone and prostaglandins 2 α to accelerate expulsion, ensure complete emptying of the uterus and prevent uterine infection.

The manufacturer does not recommend induced abortion after 45 days of pregnancy, to avoid in vivo intra-uterine fetal mummification.

The interoestrous intervals following induced abortion are usually significantly reduced by 1-3 months. The treatment does not seem to alter future reproduction in the aborted bitch.

1.2. Medical treatment of pyometra.
Repeated impregnation of the uterus by progesterone in the non-pregnant bitch during the oestrous cycle stimulates the glandular secretion of the endometrium and suppresses the contractions of the uterus, thus creating favourable environmental conditions for uterine bacterial overgrowth.

Aglepristone has been found to be an interesting medical alternative treatment of pyometra in bitches because of its marked affinity for progesterone receptors in the uterus, thus preventing the damaging effects of progesterone.

While ovario-hysterectomy remains the basic treatment for pyometra in bitches, the main indication for conservative medical treatment is pyometra in a bitch intened for breeding, in the hope of preserving her reproductive potential. Post-partum uterine infections are not an indication for aglepristone treatments.

Other indications are an old or critical bitch at high surgical risk or an owner refusing to consider surgery. In case of close pyometra, a medical treatment with aglepristone prior to surgery often helps to improve the condition of the bitch (when the cervix opens and the pus is evacuated), and therefore improves the recovery after surgery.

This treatment can be employed in case of bitches showing a serum progesterone level above 1-2 ng/mL. Aglepristone plays a role in allowing the uterine cervix to open and allowing uterine contractions leading to a discharge of the uterine content and reduction of the endometrial size. Broad spectrum antibiotics must systematically be associated during the whole duration of treatment to prevent septicemia and any other related complications.

One essential preliminary condition is the absence of peritonitis, consecutive to uterine rupture. Prior to the beginning of treatment, a careful clinical and ultrasound examination, additional blood count and biochemistry assays should be always carried out. It is very important to correct any fluid and electrolyte imbalance in the bitch. Bitches that are in anoestrus at the time of treatment (basal blood progesterone) may be more difficult to treat). When possible, it is useful to check by ultrasound that the bitch does not have any ovarian cyst, has the hormonal secretions of these cysts may increase the risk of relapse after treatment. Therefore,
such bitches should better be spayed, as they may also have further fertility problems.

The decision to proceed with medical rather than surgical treatment should be carefully weighed and the owner has to be informed about the risk of treatment failure, that would make ovario-hysterectomy necessary.

Most protocols recommend the use of aglepristone 10mg/kg at Day 1 (D1), D2, D8, D15 (eventually D29). Aglepristone may be effective alone (+ antibiotics). In case of closed-cervix pyometra, a purulent vulvar discharge was observed from 36 to 48 hours after the start of treatment, generally accompanied by a significant improvement of the general condition of the bitch.

In association, various protocols for treatment with prostaglandins F2α have proved satisfactory: cloprostenol (1μg/kg SC daily from D3 to D7, or 1 μg/kg SC on D3 and D8), dinoprost (25μg/kg SC three times daily, D3 to D7, or 25μg/kg D3,D6 and D9). Because of their uterotonic effect, prostaglandins provide faster emptying of the uterus while their specific luteolytic activity strengthens the effect of aglepristone. The addition of cloprostenol to the aglepristone therapy, compared with aglepristone alone, significantly improved the overall success rate in treating pyometra in bitches: 84.4% vs 60%.

The concomitant use of aglepristone 10mg/kg at Day 1 (D1), D2, D8, D15 (eventually D29) and misoprostol (10μg/kg per os bid D3 to D12) lead to a significant clinical improvement in 75% of the cases, without the side effects of PGF2α.

The most objective criterion of treatment efficacy is the reduction of the diameter of the uterine lumen. A decrease of the lumen of at least 50% on day 8 is seen as positive, as is the improvement in the general condition of the bitch within 48 hours.

After clinical success, in order to minimize the recurrence of pyometra, it is recommended to mate the bitch at the subsequent cycle. However, in 10-15% of the cases, bitches experience relapse in the following oestrus cycle.

1.3. Induction of parturition.

The purpose may be to induce parturition during daily periods, thus facilitating its supervision by the bitch’s owners. Some successful studies have been recently published, but only in Beagle bitches. Therefore, it is far too early to conclude about the efficacy of the following experimental procedures.

A protocol using aglepristone + oxytocin or prostaglandins F2α was described. Aglepristone (15mg/kg sc) was administered at 58 days of pregnancy in 10 bitches. Starting 24 hours later, these bitches were treated sc with either oxytocin (0.15 UI.kg) or the synthetic prostaglandin alfabrostol (0.08 mg.kg) every 2 hours until parturition. On average, parturition started 32 hours (29.7 to 34.5 hours) after aglepristone administration. In a further study using aglepristone and oxytocin with the same protocol, the onset of induced parturition in Beagle bitches occurred between 29.7 to 32 hours.
Aglepristone (15mg/kg) alone was also administered twice (9 hours interval) at 58 days of pregnancy. Expulsion of the first pup occurred between 35 and 56 h after aglepristone administration, with a mean of 41.0+/− 3.7 hours.

1.4. Planning a cesarean section.
According to some authors, the injection of 15 mg/kg 18 to 24 hours before a planned C-section may induce a final fetal maturation, thus preventing the release of premature puppies. However, further studies are needed to confirm this hypothesis.

1.5. Treatment of acromegaly.
This disease is almost always due to a progestin-induced hypersecretion of growth hormone (GH). In a recent study, preliminary data tend to show that aglepristone may be efficient in treating acromegaly in bitches.

1.6. Adverse effects
Side effects may be observed in case of aglepristone administration: restlessness, anorexia, emesis, diarrhea, drop of rectal temperature, vulvar discharge... 5.7% (5/88) bitches treated for induced abortion underwent a metritis that necessitated a specific therapy using PGF2α. (Fieni 1996).

2. Uses of antiprogestins in queens.

2.1. Induced abortion.
The dose is slightly higher than in dogs: two repeated subcutaneous injections 15 mg/kg at 24 hours interval between D0 and D45 after mating. The effectiveness of this protocol is higher before implantation (95%) than after implantation (85%). The termination of pregnancy is achieved in 50% of the queens within 3 days. In most cases, the following interoestrous interval is significantly shortened, and the queen rapidly comes in heat, with a high fertility.

2.2. Treatment of pyometra.
The combination of aglepristone and PGF2α describe above may be successfully used in queens.

3. Treatment of mammary fibroadenomatosis
Different protocols have been published:
- 20 mg/kg (SC once a week) until complete mammary regression;
- 10 mg/kg on two consecutive days, once weekly.
Usually a minimum of 4 to 6 weeks is needed for a complete mammary regression.