



GnRH Analogue Use During The Pandemic; Are We Using It Safely?



BACKGROUND

Gonadotrophin Releasing Hormone (GnRH) Analogues are used for ovarian suppression in a wide range of gynaecological pathologies. At University Hospital Wales, Prostag® - Leuprorelin Acetate is the most commonly used. Leuprorelin Acetate is currently licensed for a maximum duration of six months in endometriosis and prior to surgery for fibroids, 5-6 weeks for preoperative endometrial thinning, and is age dependent for precious puberty. It is not licensed for treatment of premenstrual dysphoric disorder and adenomyosis.

Current product guidance advises use for a maximum of six months per cycle, quoting bone loss as “not significant” in this time frame. Data suggests between a 2.3% and 15.7% bone density loss. Add-back treatment is advised by manufacturers to help limit this side effect however it has also been shown that bone mineral density dose not recover back to baseline at six years, even in combination with add-back treatment. Some data suggests Dual Energy X-Ray Absorptiometry (DEXA) scans after 24 months treatment, although the RCOG GTG. no. 48 for Pre Menstrual Syndrome advises DEXA’s annually. The British National Formulary also suggests regular liver function assessment quoting hepatic disorders as being a common side effect.

When looking for guidance on appropriate management it is evident there is no agreed upon consensus for duration or monitoring from any national body and yet with the pandemic severely impacting waiting times for definitive surgical management, the numbers of women on more than six months GnRH Analogues treatment is rising.

AIMS

- 1) Ascertain the numbers of women currently on Prostag® for all gynaecology pathologies
- 2) Assess whether we are following product and formulary guidance in respect to:
 - 1) Duration
 - 2) Add-back therapy
 - 3) DEXA scans performed at 12- 24 months.

AUDIT STANDARD

No Current National standards in circulation thus

- 1) Product guidance
- 2) GTG. 48 Pre Menstrual Syndrome
- 3) Current literature advice



Management of Premenstrual Syndrome
Greenstop Guidelines No. 48
February 2017

RESULTS

There are 114 Prostag® users. Of these the primary indications were fibroids - 53, endometriosis - 38, menorrhagia - 11, PMDD - 9, adenomyosis - 2 and pelvic congestion - 1. 61 (54%) of these women have been using Prostag® for >6 months, 51 (81%) of these for fibroids and endometriosis. Five patients used Prostag for >24 months use; 3 endometriosis, 1 fibroid, 1 PMDD. 15 of the 114 women had been using GnRH analogues for > 12 months and < 24 months. Of these patients none yet had had a DEXA scan though two have been requested for those >24 months. The average patient age is 42, 47.3 in the fibroids cohort and 34.9 in endometriosis. The range being 19-56. Of the 114 users 67 (58.8%) are taking add-back therapy. 65.5% of patients using >6 months treatment are taking add-back therapy. 60% of women using > 12 months Prostag are using add-back therapy. The number of women <45 using add-back therapy is 71.7%. 81% of women less than 45 years of age on > 6 months of Prostag® are using add-back therapy.

CONCLUSIONS

Evidence suggests that bone mineral density reduction occurs at a rate of approximately 1% per month of GnRH Analogue treatment. The risk of fracture increases 2 - 3 times with every 10% drop in density. Therefore, although add-back therapy efficacy is debated, it should always be initiated particularly in high-risk groups; this is not happening. Just 59% of patients are using add back therapy. However it does appear the younger the patient and the longer the course duration the better the rate of add back therapy use. Poor uptake maybe because of the unforeseen duration of treatment due to delayed procedures, patient choice or a lack of knowledge around prolonged use of add back therapy. It is imperative therefore that patients be appropriately counselled for the potential side effects and their implications. It is also important that advance care plans for DEXA scans are put in place for women likely to be requiring > 12-24 months of treatment. The current waiting time for a DEXA scan is a six weeks and carries a cost of approximately £150 which must be budgeted for.

This topic will be poignant for the foreseeable future as staffing and operating continue to be limited and this picture is likely to be replicated across the United Kingdom. While increasing numbers of women are being started and continued on GnRH analogues off license there continues to be no clear guidance. Moving forward we must form an agreed standard on management and monitoring of GnRH Analogues and ensure that we are adequately auditing our use.

LIMITATIONS

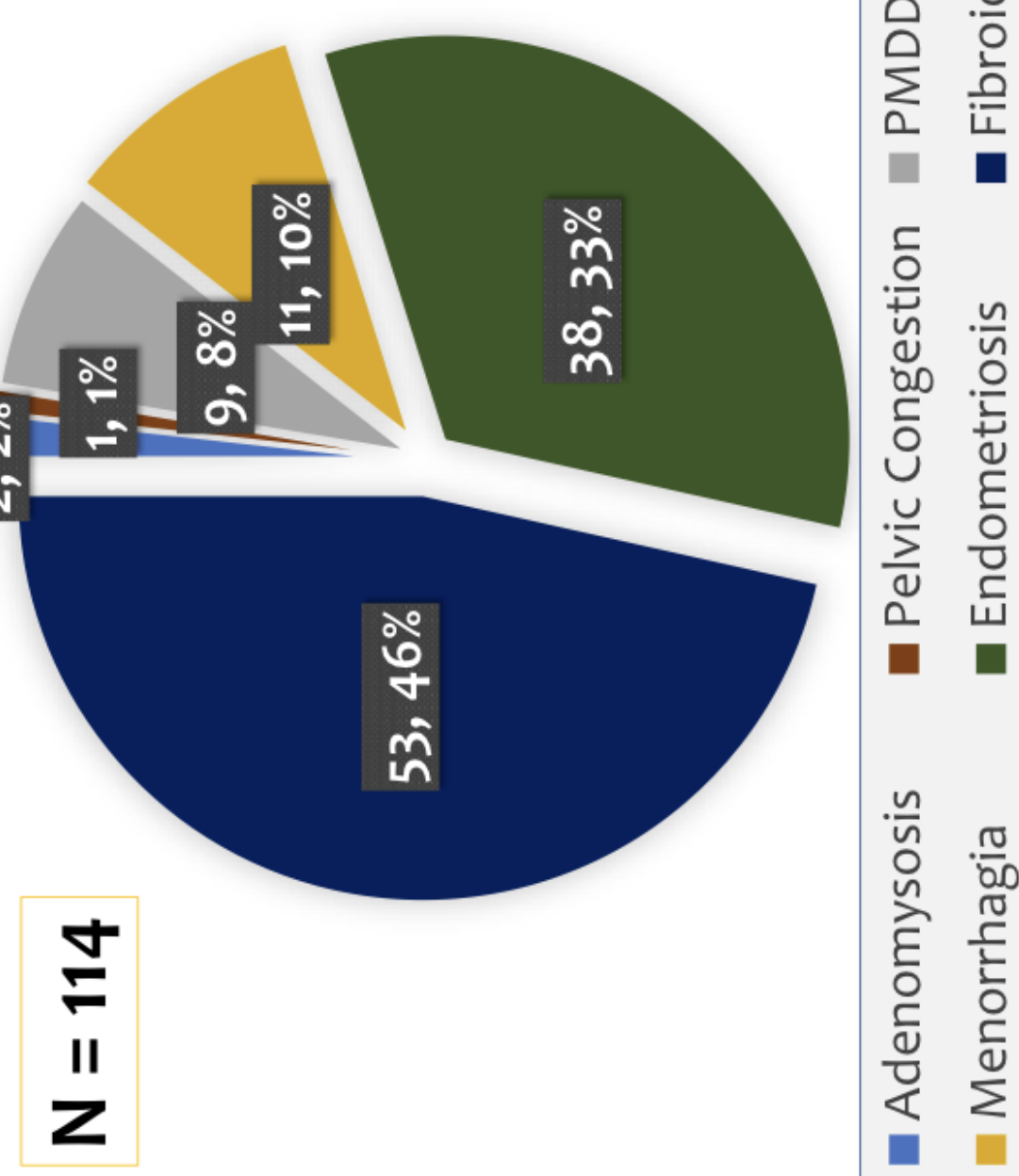
There may be some users not identified who had been receiving treatment in primary care and will not get identified using these Prostag® clinic codes. It was sometimes challenging to see from patient correspondence whether patients not on add-back therapy had been offered and declined treatment or had never been offered it. It was also difficult to assess whether there was a contraindication or reason not to go on a form of add back therapy.

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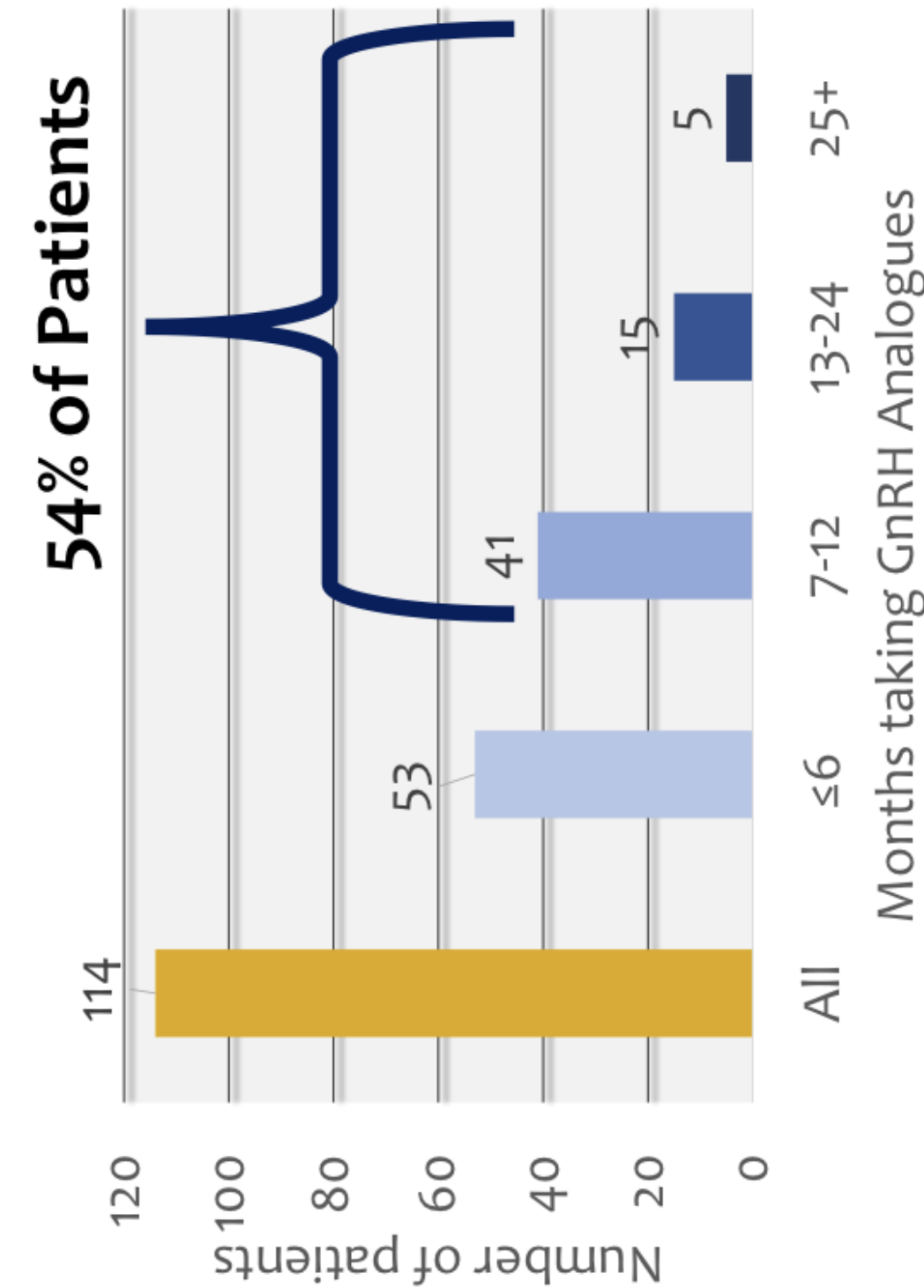
Dr. Edward Harrison, ST5 Obstetric and Gynaecology Registrar,
University Hospital Wales

Project Supervisor: Mr. Lutfi Shamsuddin, Consultant Gynaecologist,
University Hospital Wales

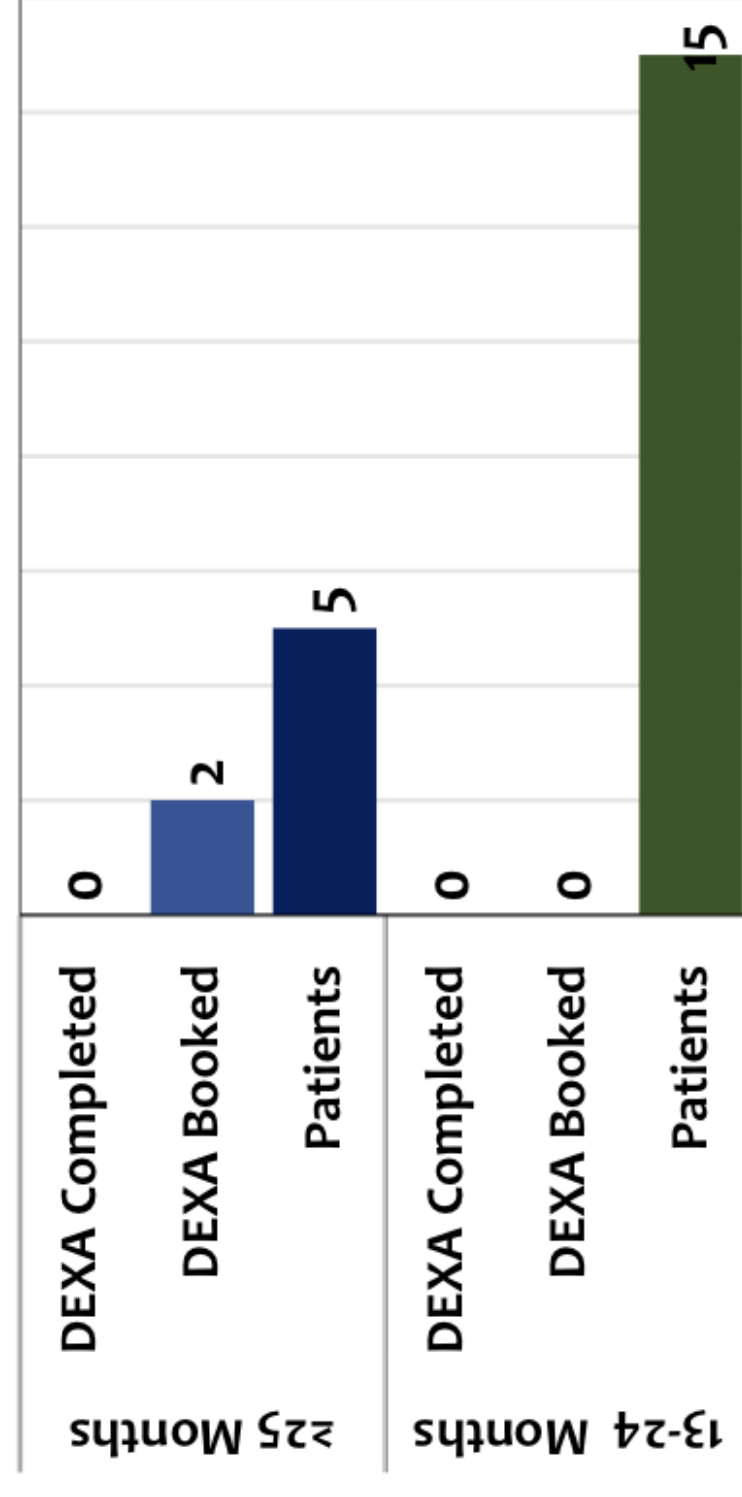
INDICATIONS FOR PROSTAP



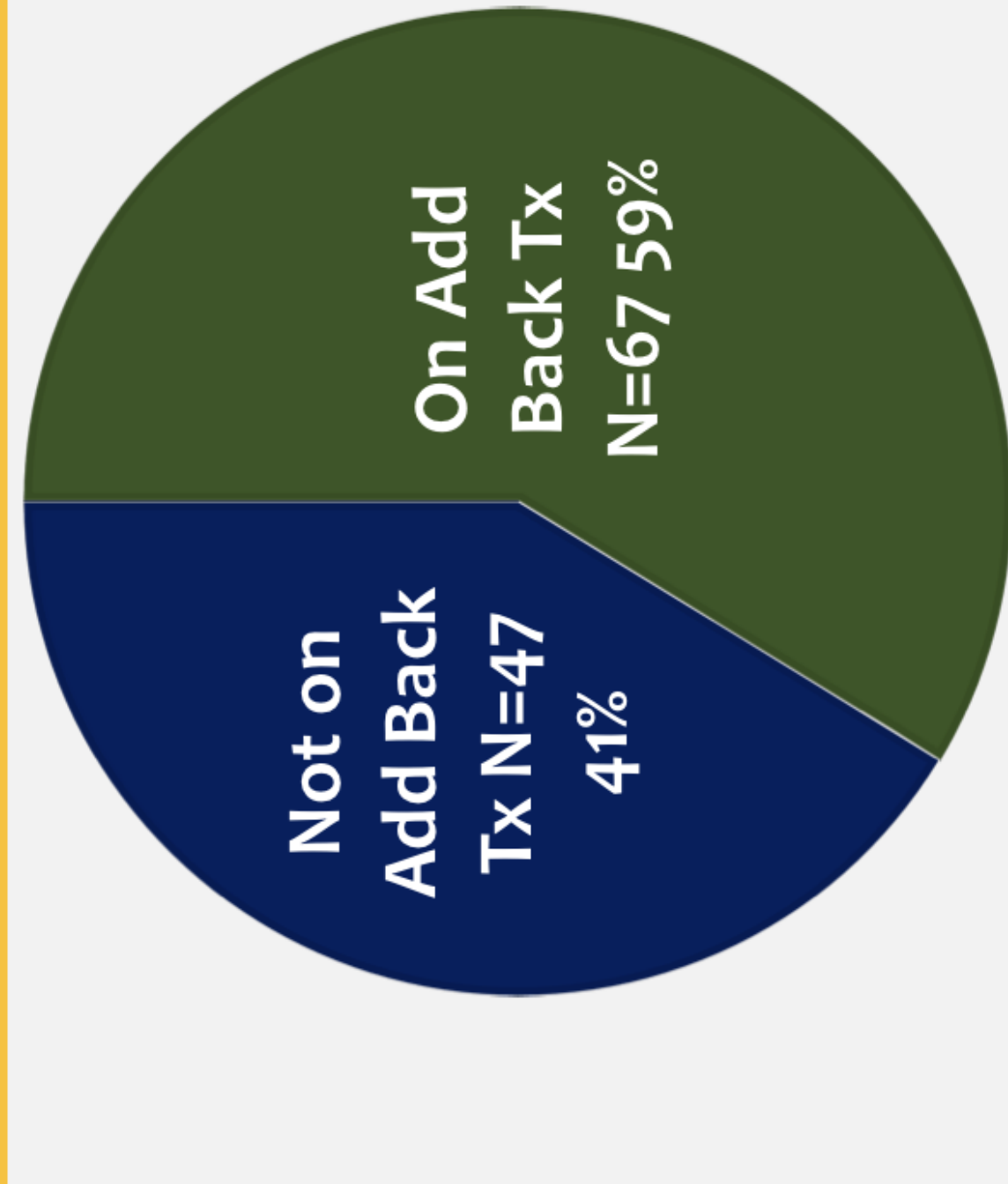
NUMBER OF PATIENTS vs DURATION



PATIENTS REQUIRING A DEXA SCAN



ADD BACK THERAPY RATE



- BOCG An International Journal of Obstetrics & Gynaecology, 2016. Management of Premenstrual Syndrome. 124(3), pp.273-2809.
- Cochrane Database of Systematic Reviews, 2016. Gonadotrophin-releasing hormone analogues for endometriosis: bone mineral density. Cochrane Database of Systematic Reviews.
- Howell, R., Edmonds, D., Dowsett, M., Cook, D., Lees, B. and Stevenson, J., 1995.
- Gonadotropin-releasing hormone analogue (gonerlin) plus hormone replacement therapy for the treatment of endometriosis: a randomized controlled trial**Supported by Zeneca Pharmaceuticals, Macclesfield, United Kingdom. Fertility and Sterility, 64(3), pp.774-481.
- Medicines.org.uk. 2022. Prostag 3 DCS 11.25-mg Powder and Solvent for Prolonged-release Suspension for Injection in Pre-filled Syringe - Summary of Product Characteristics (SmPC) - (emo). [online] Available at: <https://www.medicines.org.uk/medicine/product/465/smpc> [Accessed 7 January 2023]
- Pierce, S., Gaszoni, M. and Farquharson, R., 2006. Long-term use of gonadotropin-releasing hormone analogs and hormone replacement therapy in the management of endometriosis: a randomized trial with a 16-year follow-up. Fertility and Sterility, 74(3), pp.964-968.
- Wyatt, K., Dinmock, P., Ismail, K., Jones, P. and O'Brien, P., 2004. The effectiveness of GnRHa with and without 'add-back' therapy in treating premenstrual syndrome: a meta analysis. BJOG: An International Journal of Obstetrics and Gynaecology, 111(6), pp.585-593.

REFERENCES