



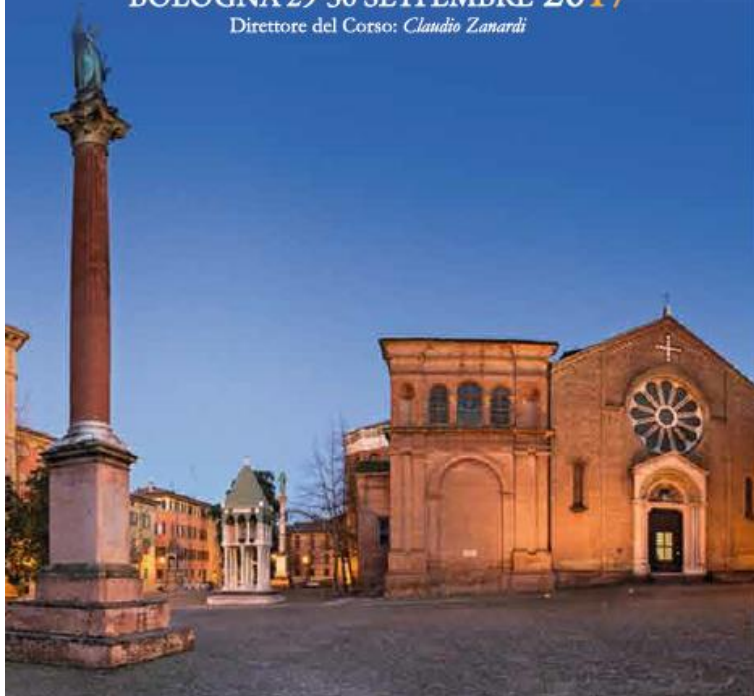
A.G.E.O.

ASSOCIAZIONE GINECOLOGI EXTRA OSPEDALIERI

CORSO DI AGGIORNAMENTO IN
GINECOLOGIA E OSTETRICIA

BOLOGNA 29-30 SETTEMBRE 2017

Direttore del Corso: *Claudio Zanardi*



TERAPIA A LUNGO TERMINE NELLA GESTIONE DELLA PAZIENTE CON MIOMI UTERINI

C. Saccardi

Dipartimento di Salute della Donna e del Bambino

Clinica Ginecologica e Ostetrica - Università degli Studi di Padova

STAR



CO - STAR



BIT PLAYER



INTRO

- 40% -60% of women of childbearing age have one or more myomas

└→ 30% symptomatic

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Overview of treatment of uterine leiomyomas (fibroids)

Author: Elizabeth A Stewart, MD

Section Editor: Robert L Barbieri, MD

Deputy Editor: Sandy J Falk, MD, FACOG

Uterine leiomyomas are benign tumors. Since histologic confirmation of the clinical diagnosis is not necessary in most cases,

asymptomatic uterine leiomyomas can usually be followed without intervention.

Women with leiomyomas whose physicians prescribed "watchful waiting" experienced no significant change in symptoms or decline in quality of life...

Moreover, evidence-based guidelines support not treating asymptomatic fibroids.

Prophylactic therapy to avoid potential future complications from myomas or their treatment is not recommended



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Am J Obstet Gynecol. Author manuscript; available in PMC 2014 October 01.

Published in final edited form as:

Am J Obstet Gynecol. 2013 October ; 209(4): 319.e1–319.e20. doi:10.1016/j.ajog.2013.07.017.

The Impact of Uterine Leiomyomas: A National Survey of Affected Women

Bijan J. Borah, PhD¹, Wanda K. Nicholson, MD, MPH, MBA², Linda Bradley, MD³, and Elizabeth A. Stewart, MD⁴

- ✓ fears, being afraid that their leiomyomas will grow
- ✓ would turn into cancer
- ✓ soiling clothes or bedding
- ✓ the negative impact on their femininity or sexuality
- ✓ uterine leiomyomas caused them to miss days of work
- ✓ uterine leiomyomas negatively impacted their career potential

**SIGNIFICANT
REDUCTION IN QoL**

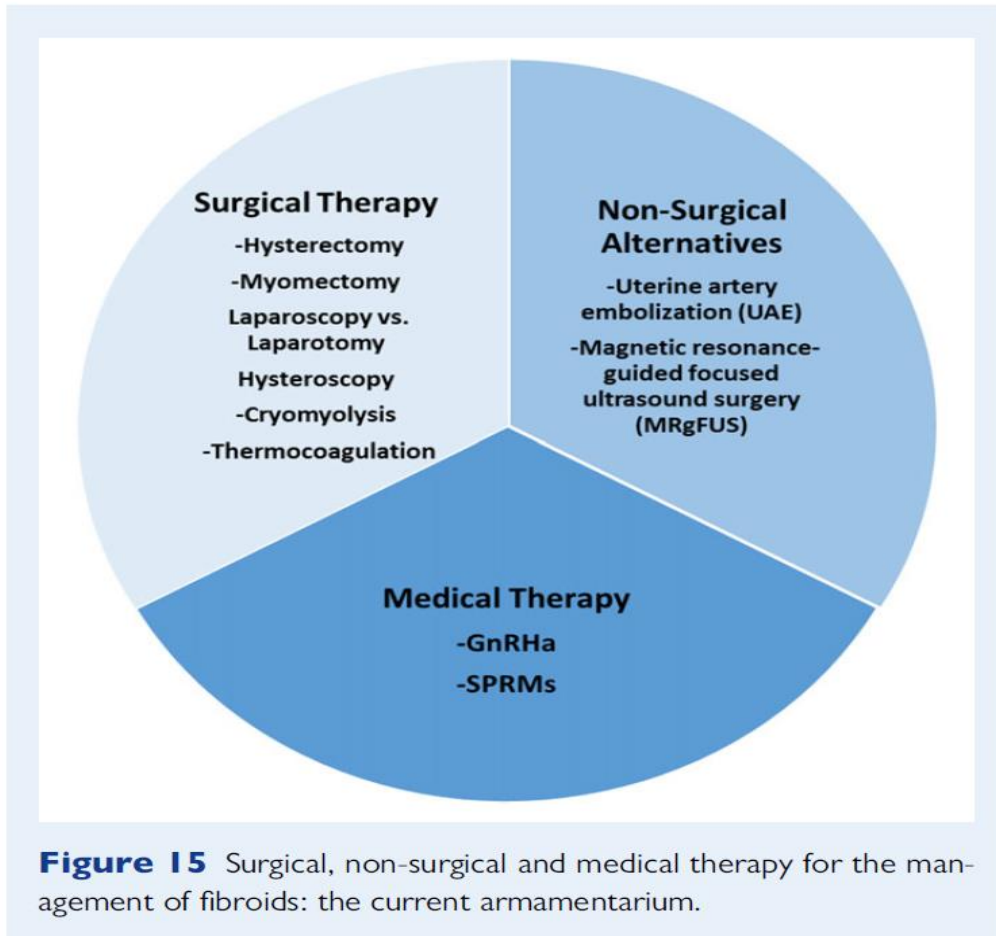
The professional and economic impact of leiomyomas is likely underestimated.

When including the costs of obstetrical outcomes related to leiomyomas, the total cost of this disease increases from \$5.9 billion to **\$34.4 billion annually in the U.S.**

TREATMENT GOALS

reduction or elimination of symptoms, through one of the following options:

- ✓ *reduction of bleeding*
- ✓ *reduction in the volume of fibroids and compressive symptoms*
- ✓ *removal of fibroids or uterus*



Human Reproduction Update Advance Access published July 27, 2016
 Human Reproduction Update, pp. 1–22, 2016
 doi:10.1093/humupd/dmw023

human
reproduction
update

GRAND THEME REVIEW

Uterine fibroid management: from the present to the future

Jacques Donnez^{1,*} and Marie-Madeleine Dolmans²

MYOMECTOMY: LPS/LPT

Arch Gynecol Obstet (2014) 290:951–956

Limits and complications of laparoscopic myomectomy: which are the best predictors? A large cohort single-center experience

Carlo Saccardi · Salvatore Gizzo · Marco Noventa ·
Emanuele Ancona · Angela Borghero ·
Pietro Salvatore Litta

Journal of Minimally Invasive Gynecology, Vol 22, No 1, January 2015

Review Article

Laparoscopic Myomectomy: Clinical Outcomes and Comparative Evidence

Victoria A. Buckley, BSc (Hons), MBBS (Hons)*,
Erin M. Nesbitt-Hawes, BMed (Hons), FRANZCOG, Paul Atkinson, BSc, MBBS,
Ha Ryun Won, MBBS, MM, FRANZCOG, Rebecca Deans, MBBS, MMed, FRANZCOG, CREI,
Alice Burton, MBBS (Hons), Stephen D. Lyons, BSc (Hons), MBBS (Hons), FRANZCOG, PhD,
and Jason A. Abbott, BMed (Hons), FRANZCOG, FRCOG, PhD

Anyway, considering very low perioperative complication rate and faster return to normal activity, LM can be considered safe and effective surgical approach remaining the gold standard one also in cases of large and intramural myomas.

morbidity, and preserving fertility remain. At laparoscopy, multiple myomas may be removed during a single procedure [25–29], and with the introduction of morcellation, myoma size is no longer the limiting factor it once was. Myomas as large as 20 cm have been removed via minimally invasive methods [30]. Power morcellation has recently come under scrutiny because of concerns about dissemination of cells from an unexpected malignant lesion [31].

CRITICAL ISSUES:

- ✓ Blood loss
- ✓ Uterine suture
- ✓ Recurrence (15-50% a 5 aa)

HYSTERECTOMY: LPS/LPT

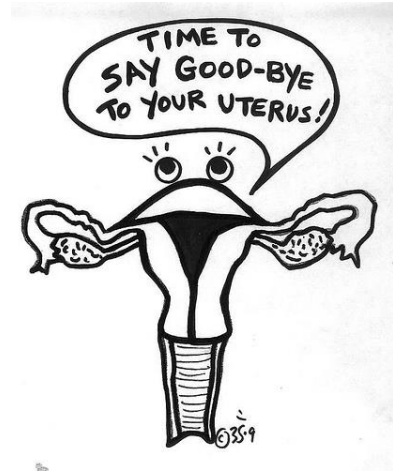
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Overview of treatment of uterine leiomyomas (fibroids)

Author: Elizabeth A Stewart, MD

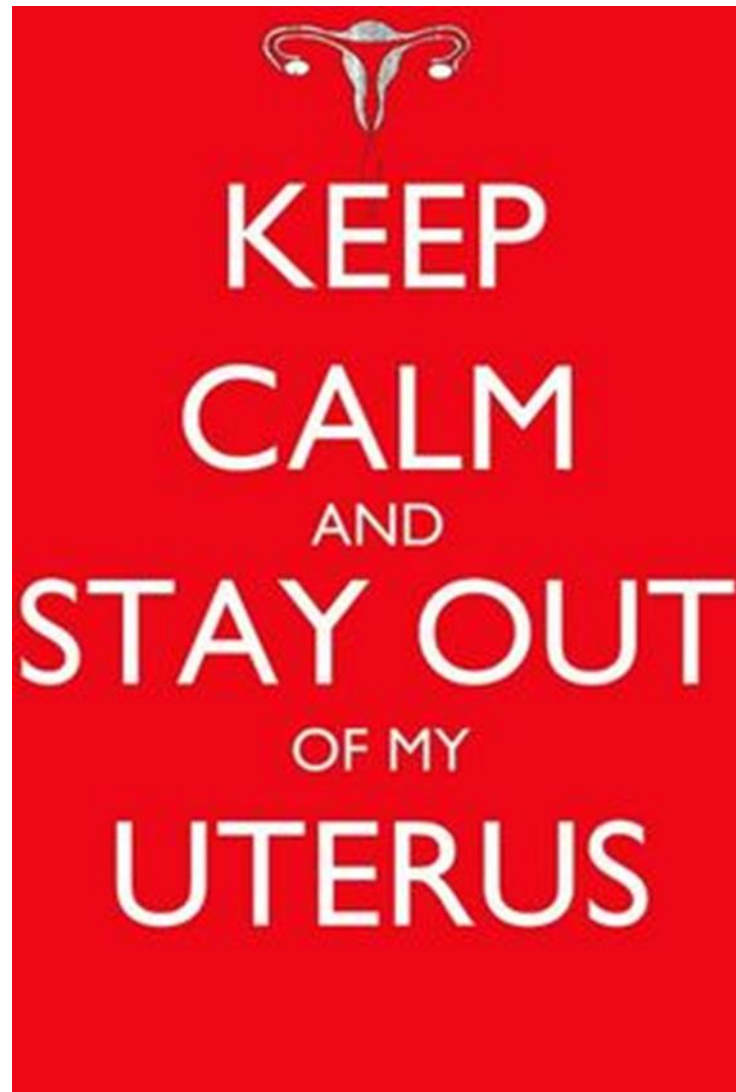
Section Editor: Robert L Barbieri, MD

Deputy Editor: Sandy J Falk, MD, FACOG



The main advantage of hysterectomy over other invasive interventions is that it eliminates both current symptoms and the chance of recurrent problems from leiomyomas.

*Leiomyomas are the most common indication for hysterectomy, accounting for **30 percent of hysterectomies in white** and over 50 percent of hysterectomies in black women [72]. The cumulative risk of a hysterectomy for leiomyomas for all women between ages 25 and 45 is 7 percent, but is 20 percent in black women*



WHAT WOMEN WANT



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The Impact of Uterine Leiomyomas: A National Survey of Affected Women

Bijan J. Borah, PhD¹, Wanda K. Nicholson, MD, MPH, MBA², Linda Bradley, MD³, and Elizabeth A. Stewart, MD⁴



Uterine-sparing treatments are important to women whether or not they were considering a pregnancy

79% feel important to have a **treatment that did not involve invasive surgery**

51% feel important to have a **treatment that allowed a woman to keep her uterus**

43% think important to have **treatment that preserved the ability to achieve pregnancy**

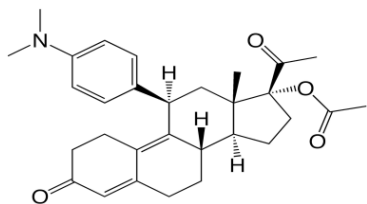
66% are concerned about missed days from work

Women verbalized the *need for information on treatment options that are non invasive* and that enable them to have children in the future.

They need to *avoid lost time at work for postoperative recuperation* so that they can continue to support themselves and their families



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alpha-acetoxy-11beta-(4-N,N-dimethylaminophenyl)-19-norpregna-4,9-diene-3,20-dione

ULIPRISTAL ACETATE

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Ulipristal Acetate versus Placebo for Fibroid Treatment before Surgery

Jacques Donnez, M.D., Ph.D., Tetyana F. Tatarchuk, M.D., Ph.D.,
Philippe Bouchard, M.D., Lucian Puscasiu, M.D., Ph.D.,
Nataliya F. Zakharenko, M.D., Ph.D., Tatiana Ivanova, M.D., Ph.D.,
Gyula Ugocsai, M.D., Ph.D., Michal Mara, M.D., Ph.D., Manju P. Jilla, M.B., B.S., M.D.,
Elke Bestel, M.D., Paul Terrill, Ph.D., Ian Osterloh, M.R.C.P.,
and Ernest Loumaye, M.D., Ph.D., for the PEARL I Study Group*

N ENGL J MED 366:5 NEJM.ORG FEBRUARY 2, 2012

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Ulipristal Acetate versus Leuprolide Acetate for Uterine Fibroids

Jacques Donnez, M.D., Ph.D., Janusz Tomaszewski, M.D., Ph.D.,
Francisco Vázquez, M.D., Ph.D., Philippe Bouchard, M.D.,
Bogusław Lemieszczuk, M.D., Francesco Baró, M.D., Ph.D., Kazem Nouri, M.D.,
Luigi Selvaggi, M.D., Krzysztof Sadowski, M.D., Elke Bestel, M.D.,
Paul Terrill, Ph.D., Ian Osterloh, M.R.C.P., and Ernest Loumaye, M.D., Ph.D.,
for the PEARL II Study Group*

N ENGL J MED 366:5 NEJM.ORG FEBRUARY 2, 2012



3-month cycle
5 mg UPA

- **90% bleeding reduction**
- **30% volume reduction**



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They need to avoid lost time at work for postoperative recuperation so that they can continue to support themselves and their families

SEMINAL CONTRIBUTIONS

Long-term treatment of uterine fibroids with ulipristal acetate[☆]

Jacques Donnez, M.D.,^a Francisco Vázquez, M.D.,^b Janusz Tomaszewski, M.D.,^c Kazem Nouri, M.D.,^d Philippe Bouchard, M.D.,^e Bart C. J. M. Fauser, M.D.,^f David H. Barlow, F.R.C.O.G.,^g Santiago Palacios, M.D.,^h Olivier Donnez, M.D.,ⁱ Elke Bestel, M.D.,^j Ian Osterloh, M.R.C.P.,^k and Ernest Loumaye, M.D.,^l for the PEARL III and PEARL III Extension Study Group

Fertility and Sterility® Vol. 101, No. 6, June 2014

Long-term medical management of uterine fibroids with ulipristal acetate

Jacques Donnez, M.D.,^a Olivier Donnez, M.D.,^b Dace Matule, M.D.,^c Hans-Joachim Ahrendt, M.D.,^d Robert Hudeček, M.D.,^e Janos Zatik, M.D.,^f Zaneta Kaslovska, M.D.,^g Mihai Cristian Dumitrascu, M.D.,^h Hervé Fernandez, M.D.,ⁱ David H. Barlow, F.R.C.O.G.,^j Philippe Bouchard, M.D.,^k Bart C. J. M. Fauser, M.D.,^l Elke Bestel, M.D.,^m and Ernest Loumaye, M.D.,ⁿ

Fertility and Sterility® Vol. 105, No. 1, January 2016

AGENZIA ITALIANA DEL FARMACO

DETERMINA 14 settembre 2016

Regime di rimborsabilità e prezzo a seguito di nuove indicazioni terapeutiche del medicinale per uso umano «Esimya». (Determina n. 1227/2016). (26A07033)

(GU n.231 del 3-10-2016)

Classificazione ai fini della rimborsabilità

Le nuove indicazioni terapeutiche:
Ulipristal acetato e' indicato nel trattamento intermittente dei sintomi da moderati a gravi di fibromi uterini in donne adulte in età riproduttiva.
del medicinale sono rimborsate come segue:
Confezione:
«5 mg - compressa - uso orale - blister (ALU/PVC/PE/PVDC)» 28 compresse - A.I.C. n. 042127013 (in base 10) 186P85 (in base 32).
Classe di rimborsabilità: A Nota 51.

Classificazione ai fini della fornitura

La classificazione ai fini della fornitura del medicinale ESIMYA e' la seguente:
Medicinale soggetto a prescrizione medica limitativa, da rinnovare volta per volta, vendibile al pubblico su prescrizione di centri ospedalieri o di specialisti - ginecologo (RNL).

art. 3

Condizioni e modalita' di impiego

Prescrizione del medicinale soggetta a diagnosi - piano terapeutico e a quanto previsto dall'allegato 2 e successive modifiche, alla determinazione 29 ottobre 2004 - PNT Prontuario della distribuzione diretta - pubblicata nel supplemento ordinario alla Gazzetta ufficiale n. 259 del 4 novembre 2004.

IDEAL TREATMENT

- ✓ Easy to use
- ✓ 100% effective
- ✓ Harmless
- ✓ Free of side effects
- ✓ Cost-effective



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They need to *avoid lost time at work for postoperative recuperation* so that they can continue to support themselves and their families

EASY TO USE

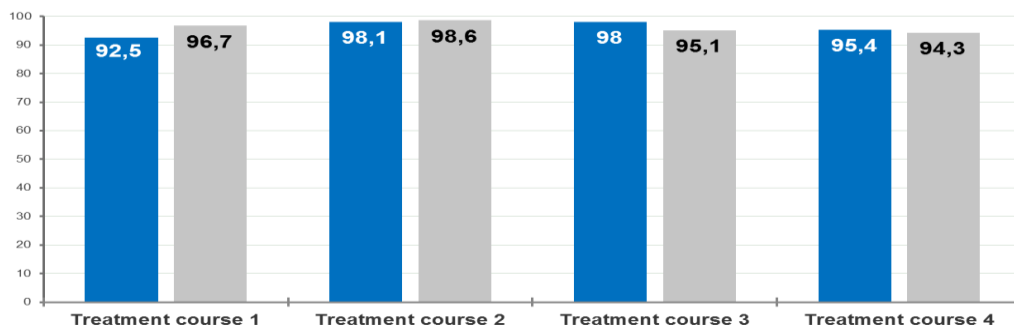




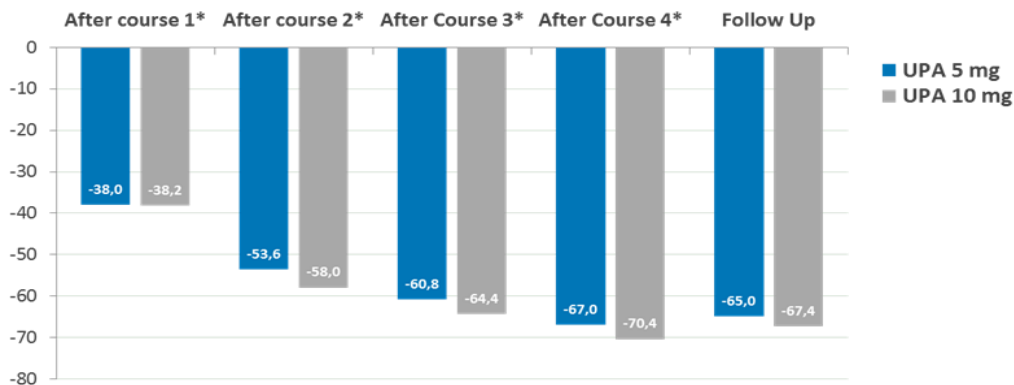
Women verbalized the need for information on *treatment options that are non invasive* and that enable them to have children in the future.
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EFFECTIVE

patients with control of bleeding at the end of each treatment cycle (%)



reduction in the volume of fibroids (%)



Long-term medical management of uterine fibroids with ulipristal acetate

Jacques Donnez, M.D.,^a Olivier Donnez, M.D.,^b Dace Matule, M.D.,^c Hans-Joachim Ahrendt, M.D.,^d Robert Hudecek, M.D.,^e Janos Zatik, M.D.,^f Zaneta Kaslovskeiene, M.D.,^g Mihai Cristian Dumitrascu, M.D.,^h Hervé Fernandez, M.D.,ⁱ David H. Barlow, F.R.C.O.G.,^j Philippe Bouchard, M.D.,^k Bart C. J. M. Fauser, M.D.,^l Elke Bestel, M.D.,^m and Ernest Loumaye, M.D.ⁿ

Fertility and Sterility® Vol. 105, No. 1, January 2016

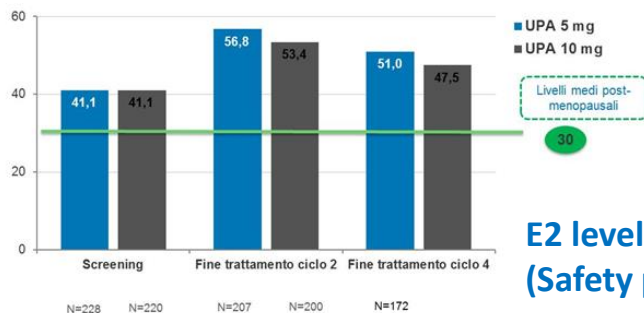


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SIDE EFFECTS

Headache and headache are the most frequent adverse events (less than 10%) after the first 3 months of therapy, they tend to decrease in the following months

AE, N. patients (%)	Course 1		Course 2		Course 3		Course 4	
	UPA 5 mg (N=230)	UPA 10 mg (N=221)	UPA 5 mg (N=215)	UPA 10 mg (N=205)	UPA 5 mg (N=193)	UPA 10 mg (N=188)	UPA 5 mg (N=180)	UPA 10 mg (N=174)
Patients with ≥1 AE	47 (20.4)	43 (19.5)	28 (13.0)	22 (10.7)	9 (4.7)	12 (6.4)	11 (6.1)	14 (8.0)
Headache	10 (4.3)	10 (4.5)	6 (2.8)	0	3 (1.6)	2 (1.1)	1 (0.6)	2 (1.1)
Hot flashes	12 (5.2)	14 (6.3)	8 (3.7)	6 (2.9)	3 (1.6)	5 (2.7)	5 (2.8)	7 (4.0)
Fatigue	2 (0.9)	5 (2.3)	2 (0.9)	1 (0.5)	0	1 (0.5)	0	1 (0.6)
Acne	4 (1.7)	4 (1.8)	2 (0.9)	1 (0.5)	1 (0.5)	0	0	0



E2 levels during the study
(Safety population)

Long-term medical management of
uterine fibroids with ulipristal acetate

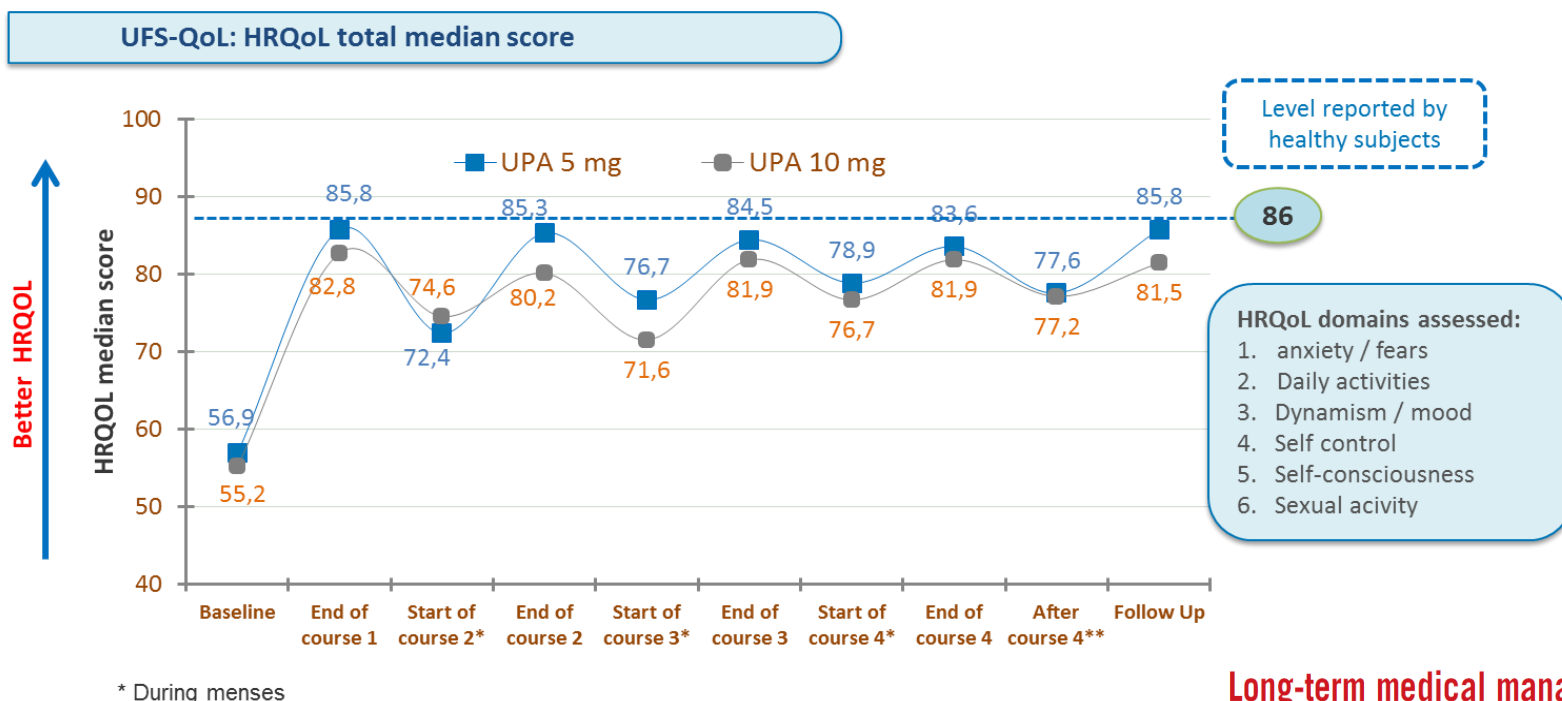
Jacques Donnez, M.D.,^a Olivier Donnez, M.D.,^b Dace Matule, M.D.,^c Hans-Joachim Ahrendt, M.D.,^d Robert Hudecek, M.D.,^e Janos Zatik, M.D.,^f Zaneta Kaslovskeiene, M.D.,^g Mihai Cristian Dumitrascu, M.D.,^h Hervé Fernandez, M.D.,ⁱ David H. Barlow, F.R.C.O.G.,^j Philippe Bouchard, M.D.,^k Bart C. J. M. Fauser, M.D.,^l Elke Bestel, M.D.,^m and Ernest Lomay, M.D.ⁿ

Fertility and Sterility® Vol. 105, No. 1, January 2016



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UPA BRING BACK TO A NORMAL QUALITY OF LIFE



Long-term medical management of uterine fibroids with ulipristal acetate

Jacques Donnez, M.D.,^a Olivier Donnez, M.D.,^b Dace Matule, M.D.,^c Hans-Joachim Ahrendt, M.D.,^d Robert Hudecek, M.D.,^e Janos Zatik, M.D.,^f Zaneta Kaslovska, M.D.,^g Mihai Cristian Dumitrascu, M.D.,^h Hervé Fernandez, M.D.,ⁱ David H. Barlow, F.R.C.O.G.,^j Philippe Bouchard, M.D.,^k Bart C. J. M. Fauser, M.D.,^l Elke Bestel, M.D.,^m and Ernest Loumaye, M.D.ⁿ

Fertility and Sterility® Vol. 105, No. 1, January 2016



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WHAT ABOUT THE POSSIBILITY OF FUTURE PREGNANCIES?

First series of 18 pregnancies after ulipristal acetate treatment for uterine fibroids

Mathieu Luyckx, M.D.,^a Jean-Luc Squifflet, M.D., Ph.D.,^a Pascale Jadoul, M.D.,^a Raffaella Votino, M.D.,^a Marie-Madeleine Dolmans, M.D., Ph.D.,^{a,b} and Jacques Donnez, M.D., Ph.D.^c

Fertility and Sterility® Vol. 102, No. 5, November 2014

Twenty-one patients attempted to get pregnant, among whom 15 (71%) succeeded, totaling 18 pregnancies. Among these 18 pregnancies, 12 resulted in the birth of 13 healthy babies and 6 ended in early miscarriage.

No regrowth of fibroids was observed during pregnancy

Our data confirm a sustained long-term effect after UPA therapy



Women verbalized the need for information on treatment options that are non invasive and that enable them to have children in the future.
They need to avoid lost time at work for postoperative recuperation so that they can continue to support themselves and their families

COST-EFFECTIVENESS

TABLE III.—*Nationwide prediction of future expenditure for repeated-intermittent use with UPA 5 mg.*

	Drug-costs for the NHS with repeated-intermittent cycles of UPA 5 mg (million €)	Surgery costs for the NHS with repeated-intermittent cycles of UPA 5 mg (million €) **	Total costs for the NHS with repeated-intermittent cycles of UPA 5 mg (million €)	Total costs for the NHS with pre-surgical treatment of UPA 5 mg (million €)	Saving for the NHS (million €)
Repeated-intermittent UPA 5 mg (4 cycles)	35.5 *	27.3 §	62.8		26
Repeated-intermittent UPA 5 mg (6 cycles)	51.6 *	19.6 §§	71.2	88.8 ##	17.6
Repeated-intermittent UPA 5 mg (8 cycles)	68 *	11.9 §§§	79.9		8.9
Repeated-intermittent UPA 5 mg (10 cycles)	84.4 *	4.2 #	88.6		0.2

MINERVA
GINECOLOGICA

VOL. 68 • N. 1 • PAG. 15/20 • FEBRUARY 2016

REPEATED-INTERMITTENT USE
OF ULIPRISTAL ACETATE
FOR THE MANAGEMENT OF UTERINE FIBROIDS:
AN ITALIAN PHARMACOECONOMIC EVALUATION

G. MARATA



Medical therapy with 5 mg UPA is cost effective compared to the pre-surgical therapy

The potential savings, is reported to be 26 million € with the long-term use of UPA 5 mg

Heavy menstrual bleeding: assessment and management

Fibroids 3 cm or more in diameter

- 1.5.11 Offer ulipristal acetate 5 mg (up to 4 courses)^[5] to women with heavy menstrual bleeding and fibroids of 3 cm or more in diameter, and a haemoglobin level of 102 g per litre or below. [new 2016]
- 1.5.12 Consider ulipristal acetate 5 mg (up to 4 courses)^[5] for women with heavy menstrual bleeding and fibroids of 3 cm or more in diameter, and a haemoglobin level above 102 g per litre. [new 2016]

RESEARCH ARTICLE

Safety after extended repeated use of ulipristal acetate for uterine fibroids

Bart C. J. M. Fauser^{1☯*}, Jacques Donnez^{2‡}, Philippe Bouchard^{3‡}, David H. Barlow^{4‡}, Francisco Vázquez^{5‡}, Pablo Arriagada^{6☯}, Sven O. Skouby^{7‡}, Santiago Palacios^{8‡}, Janusz Tomaszewski^{9‡}, Boguslaw Lemieszczuk^{10‡}, Alistair R. W. William^{11‡}

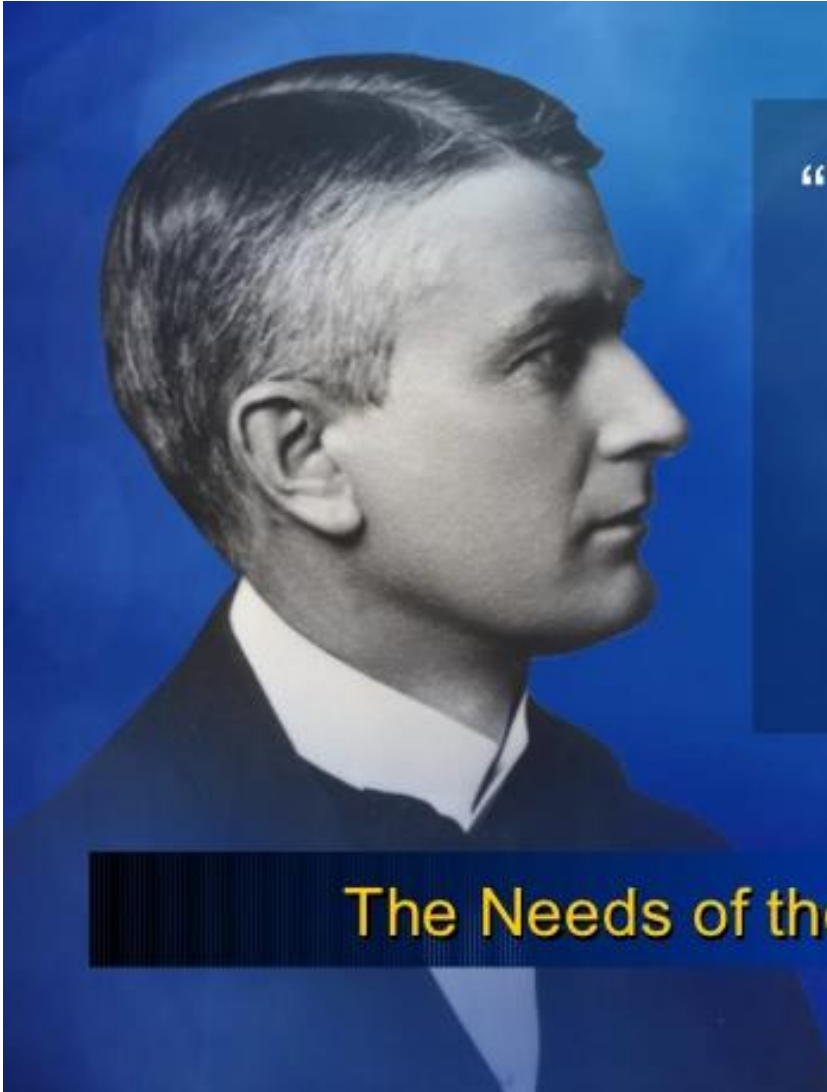
PLOS ONE | DOI:10.1371/journal.pone.0173523 March 7, 2017

Table 2. Summary of endometrium biopsy consensus and endometrium biopsy non-physiological descriptions (PAEC) (Full analysis set, N = 64).

	Screening	After course 4	After Course 8	3-month after course 8
Total Biopsies	52	61	48	24
Adequate Biopsies (^{1*})	50 (96.2%)	56 (91.8%)	43 (89.6%)	22 (91.7%)
Benign (^{2**})	50 (100%)	56 (100%)	43 (100%)	22 (100%)
Hyperplasia (^{2**})	0	0	0	0
Malignant neoplasm (^{2**})	0	0	0	0
Non-physiological changes observed by two or three pathologists**	9 (18.0%)	12 (21.4%)	7 (16.3%)	2 (9.1%)

Table 3. Summary of laboratory parameters (Full analysis set, N = 64).


Parameter (unit), normal range	Screening		After course 4		3 months post treatment course 4		After course 8	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
Hemoglobin (g/dL), 11.5–15.5	63	12.8 ± 1.57	64	13.0 ± 1.36	63	12.8 ± 1.34	48	13.3 ± 0.95
Creatinine (umol/L), 45–84	63	61.4 ± 8.5	64	60.8 ± 8.6	63	63.0 ± 10.0	48	64.3 ± 9.8
Total bilirubin (umol/L), 0–19	63	6.5 ± 3.3	64	7.0 ± 3.6	63	7.1 ± 3.9	47	7.3 ± 3.0
AST (U/L), 0–37	63	21.3 ± 5.0	64	20.5 ± 4.5	63	21.1 ± 6.6	48	19.5 ± 4.8
ALT (U/L), 0–47	63	18.6 ± 6.7	64	16.0 ± 6.1	63	17.2 ± 10.6	48	16.8 ± 6.6
Total Cholesterol (mmol/L), 0–5.17	63	5.3 ± 0.79	60*	5.5 ± 0.82*	63	5.3 ± 0.72	49	5.3 ± 0.94
HDL (mmol/L), 1.04–25.88	63	1.7 ± 0.36	60*	1.7 ± 0.41*	63	1.7 ± 0.38	49	1.7 ± 0.35
LDL (mmol/L), 0–2.58	62	3.1 ± 0.73	60*	3.3 ± 0.79*	63	3.1 ± 0.70	49	3.1 ± 0.84
Triglycerides (mmol/L), 0–1.69	63	1.3 ± 0.88	60*	1.2 ± 0.73*	63	1.1 ± 0.70	49	1.3 ± 0.82

A black and white profile portrait of William J. Mayo, MD, facing right. He is wearing a dark suit jacket over a white shirt and a dark tie. The background is a solid blue color.

“The best interest
of the patient
is the only interest
to be considered”

William J. Mayo, MD

The Needs of the patient come first

The Mayo Clinic logo, featuring a stylized 'M' and 'C' inside a shield-like shape, followed by the text 'MAYO CLINIC' in a serif font.

MAYO CLINIC

