



Delivery of Pharmacogenetics results to patients in Europe

Delivery of Pharmacogenomics Test Results in Patient Care
ASCPT annual meeting 2018



LEIDEN UNIVERSITY
MEDICAL CENTER



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Ubiquitous Pharmacogenomics

Making actionable pharmacogenomic data and effective treatment optimization accessible to every European citizen

Call identifier : H2020-PHC-24-2015-two-stage
Proposal No: 668353-I
Acronym: U-PGx



U - PGx | Ubiquitous Pharmacogenomics

- **Funded by EU Horizon 2020 (€15 million)**
- **Start 1-1-2016**
- **5 year project**
- **Implement preemptive PGx testing in a real world setting across 7 European sites**
 - Using the DPWG guidelines to guide drug and dose selection
- **Evaluate patient outcome and cost effectiveness in a RCT**





MARK J. RATAIN

U. of Chicago, USA



RUSS ALTMAN

Stanford University, Stanford, CA, USA



DAN RODEN

Vanderbilt University School of Medicine,
Nashville, TN, USA



MARY RELLING

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MICHEL EICHELBAUM

Dr. Margarete Fischer-Bosch-Institute of
Clinical Pharmacology, Stuttgart, DE



DAVID H.U. HAERRY

Patient and Consumer Working Party of the
European Medicines Agency (EMA), Bern,
Switzerland

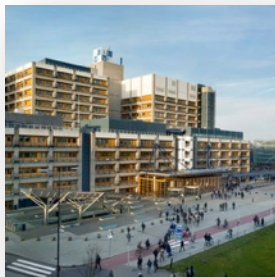
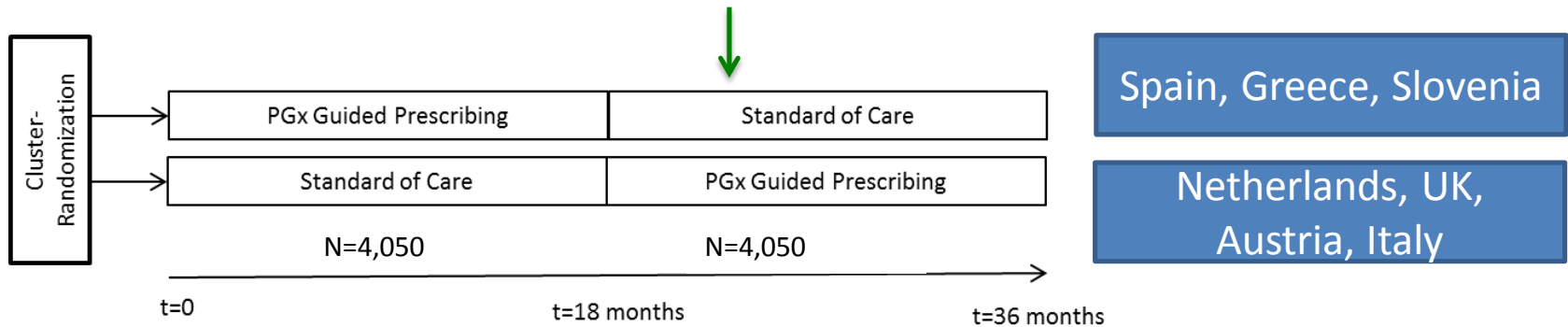
David Haerry joins U-PGx advisory board

Posted on *August 17, 2016* by *Angeliki Rapti*

David Haerry is a patients' advocate. He is a member of the European AIDS Treatment Group (EATG). David has been involved in HIV drug development for many years and has specific interests in the areas of Personalised Medicine, Risk Communication and Doctor/Patient Communication, Pharmacovigilance, Observational Studies, Biomedical Prevention and HIV Eradication Research.

PREemptive Pharmacogenomic testing for preventing Adverse drug Reactions (PREPARE)

New set of patients



- N=8,100
- 30% reduction clinically relevant ADRs

Each site has its own therapeutic focus



Development of barrier-free CDSS



safety-code
The Medication Safety Code initiative

What is it?
The Medication Safety Code on the left represents a patient-specific genetic profile regarding important pharmacogenes.

How does it work?
After scanning the QR code (e.g. with a smartphone), you are led to a website that displays patient-specific drug dosing recommendations.

Laboratory contact
+0123456789
Some lab name
Some street name 123/45
1234 Some city name

www.safety-code.org



Scan QR code



Filter substance list...

Critical for this patient

− Azathioprine (!)

Dutch Pharmacogenetics Working Group guideline

Reason: TPMT poor metabolizer
Select alternative drug or reduce dose by 90%. Increase dose in response of hematologic monitoring and efficacy.
Date of evidence: March 10, 2011

Show guideline website

+ Codeine (!)

+ Mercaptopurine (!)

+ Thioguanine (!)



Dr. Matthias Samwald

safety-code Name: Jane Doe
The Medication Safety Code initiative Date of birth: 01.02.1934

Gene, status	Critical drug substances (modification recommended!)
CYP2C19 Poor metabolizer	Clopidogrel, Sertraline
CYP2D6 Ultrarapid metabolizer	Amitriptyline, Aripiprazole, Clomipramine, Codeine, Doxepin, Haloperidol, Imipramine, Metoprolol, Nortriptyline, Paroxetine, Propafenone, Risperidone, Tamoxifen, Tramadol, Venlafaxine
TPMT Poor metabolizer	Azathioprine, Mercaptopurine, Thioguanine
Other genes Not actionable	ABCB1, ADRB1, BRCA1, COMT, CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP3A4, CYP3A5, DPYD, G6PD, HMGCR, P2RY12, SULT1A1, UGT1A1, VKORC1

Date printed: 10.12.2015 Card number: 0000001

<http://safety-code.org/>

[J Am Med Inform Assoc.](https://doi.org/10.1093/jamia/ocy005) 2018 Feb 9. doi: 10.1093/jamia/ocy005. [Epub ahead of print]

Full integration in EMR....

LU
MC

Dutch PGx Working Group (DPWG) guidelines (N=84)

CYP2D6		CYP2C9		CYP2C19	
• Amitriptyline	• Metoprolol	• Acenocoumarol	• Citalopram	• Clopidogrel	
• Aripiprazol	• Mirtazapine	• Phenprocoumon	• Imipramine	• Lansoprazol	
• Atomoxetine	• Nortriptyline	• Phenytoin			
• Carvedilol	• Olanzapine	• Glibenclamide			

Table 2. Availability of pharmacogenetic test results at general practitioners' practices and community pharmacies.

Test results still available?	General practitioner		Community pharmacy		General practitioner or community pharmacy, number (%)	General practitioner and community pharmacy, number (%)
	Number (%)	p-value [†]	Number (%)	p-value [†]		
EM	0/101 (0.0)	0.010*	0/95 (0.0)	0.001*	0/82 (0.0)	0/82 (0.0)
Non-EM	6/90 (6.7)		11/92 (12.0)		3/80 (3.8)	6/74 (7.5)
Total	6/191 (3.1%)		11/187 (5.9%)		3/162 (1.9%)	6/162 (3.7%)

[†]*Compared to non-EM; p < 0.05 is considered significant.

From Pearson χ^2 or Fisher's exact test – whichever was appropriate.

EM: Extensive metabolizer.

[1. Pharmacogenomics.](#) 2017 Jun;18(9):843-851

..... only **3.1%** GPs and **5,9%** of the pharmacies were able to retrieve CYP2D6 genotyping results¹



Patient Education

Agenda WP4 TC 16032018 - jesse.swen@gmail.com... Outlook Web App F5 Dynamic Webtop Ubiquitous Pharmacogenomics (U-PGx) | Making...

U-PGx | Ubiquitous Pharmacogenomics

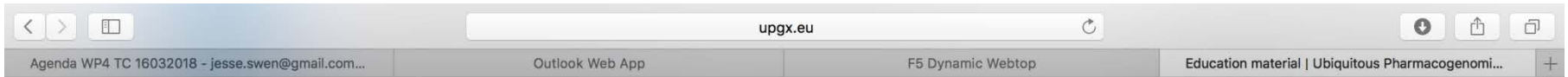
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**WE WANT TO MAKE EFFECTIVE
TREATMENT OPTIMIZATION
ACCESSIBLE TO EVERY EUROPEAN
CITIZEN**

[TELL ME MORE](#)



Patient Education



U-PGx e-learning platform

Posted on April 24, 2017 by Angeliki Rapti

Here you can find a [link](#) to an e-learning program for the participating healthcare professionals in the implementation sites addressing goals and topics of interest of PGx knowledge. [Continue reading →](#)

Posted in *Education material*

... with sunitinib-treated cancer

- 3rd UPGx Personalized Medicine Day
- H.E. the United States Ambassador in Greece visits UPAT and gets informed about the U-PGx project



U-PGx | Ubiquitous Pharmacogenomics Video

Posted on October 4, 2016 by Wendy van Hemmen

This U-PGx video (6 minutes) visualises and promotes the idea of personalised medicine and pre-emptive PGx testing. The video can be used to inform the public via the webpage, for educational purpose and for communication with stakeholders and at (inter)national workshops. [Continue reading →](#)

Posted in *Education material*



How Genetic testing can be used to personalized drug prescriptions and dosages

Posted on June 23, 2016 by Manolis Viennas



Patient Education

1st UPGx Personalized Medicine Public Day, London, UK



06.Dec.17

8:30 am - 8:30 pm
London, UK

U-PGx | Ubiquitous Pharmacogenomics



One of the most important prerequisites of the successful implementation of pharmacogenomics into the clinic is the increase of the general public's awareness over the benefits of pharm...

Recognizing this f...
Personalized Medi...
Medicine availabl...
afternoon of Dece...
outreaching activi...
European Commis...

This event is near...
policy makers.

Registration is FR...
free.

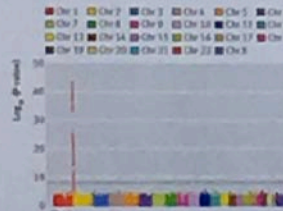
On behalf of the O...

Q1: After eating asparagus, does your urine have a strange smell?

Yes
No



Sniffing out significant "Pee values": genome wide association study of asparagus anosmia



- 58% of men and 61% of women cannot smell asparagus metabolites in urine
- Variation in the gene for olfactory receptor 2



UNIVERSITY OF
LIVERPOOL

THE WOLFSON
CENTRE FOR
PERSONALISED
MEDICINE

"a few stems of asparagus eaten, shall give our urine a disagreeable odour".
Benjamin Franklin 1781

Prof. Munir Pirmohamed



U-PGx | Ubiquitous Pharmacogenomics



Patient interest and belief in PGx

“I am familiar with PGx

19.9% Agrees

**“PGx contributes to reducing
the severity and frequency of
side-effects”**

83.6% Agrees

**“I would like to learn more
about PGx”**

70.2% Agrees

**“I would like my PGx profile to
be tested before starting a
drug”**

81.8% Agrees



Patients understanding of PGx and their Safety-Code Card

- “When I am prescribed a new drug it is important to inform my doctors about my PGx profile”*

86.4% Agrees

- “I feel I have received sufficient information to understand my PGx results”*

86.8% Agrees




safety-code
The Medication Safety Code initiative

I participate in the U-PGx PREPARE study (study arm). For more information, please visit www.upgx.eu/study

To the healthcare provider:
Please scan the QR code to view pharmacogenomics-based drug dosing recommendations for this patient.

Contact
Lab name
E-mail address
Phone
Additional contact information

U-PGx



safety-code
The Medication Safety Code initiative

Name: Jane Doe
Date of birth: 01.02.1934

Gene, status	Critical drug substances (modification recommended)
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TPMT Poor metabolizer	Azathioprine, Mercaptopurine, Thioguanine
Other tested genes Not actionable	CYP2B6, CYP2C9, CYP3A5, DPYD, F5, HLA-A3101, HLA-B1502, HLA-B5701, SLCO1B1, TPMT, UGT1A1, VKORC1

Date printed: 15.06.2017



Points for discussion

- Patients are highly (too?) optimistic about PGx
- There is a clear demand for more education
- Distribution of PGx test results across different healthcare systems is challenging – the patient can help



Thank you for your attention!



Clin Pharmacol Ther.
2017 101(3):341-358.

U-PGx Kick-off Leiden Jan 19th, 2016

www.upgx.eu

Email: j.j.swen@lumc.nl

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 668353



U-PGx | Ubiquitous Pharmacogenomics



Data collection: Lareb Intensive Monitoring (LIM) Survey

The screenshot displays the U-PGx website interface. At the top, there is a navigation bar with 'U-PGx' and 'Home Log in'. The main content area features a large image of a child with arms raised. Below the image, there are three columns of text: 'Background information', 'Information about participation', and 'Contact information'. A blue box on the left contains login and participation options. A large blue box on the right contains the survey title in Greek: 'Καλώς ήρθατε στην διαδικτυακή έρευνα της μελέτης PREPARE!'. Below this, there are several orange buttons: 'Welcome', 'Side-effect', 'Quality of life', 'Attitudes towards pharmacogenomics', and 'Completion'. At the bottom, there is a section titled '* All questions are mandatory' and a welcome message in English: 'Welcome to the PREPARE Study online survey! This survey will pose questions regarding your experiences with the drug: {{U-PGx medicine.surveymedicine}}, which you have started using 2 weeks ago. If you have stopped using this medication, please still fill in this survey.'

- Patient are able to report adverse events directly, without the intervention of a HCP
- Surveys are translated into local languages



Lareb Intensive Monitoring (LIM) response rates

- 29.6% (n=635) of participants are registered

Country	Number of registrations	% of National enrolment
Netherlands	362	85,6%
United Kingdom	57	16,9%
Italy	5	1,3%
Austria	51	53,7%
Spain	38	11,7%
Greece	24	6,9%
Slovenia	98	54,4%

