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3.2 Study of liver function monitoring in patients receiving agomelatine using the Estonian Health Insurance Fund (EHIF) database

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WHY?

HOW?

WHAT?

SO?

WHY?

- CAP, authorised in 2009 for the treatment of major depressive episodes in adults
- Risk of liver injury known from the start
- Warning in the SPC – liver function monitoring before the treatment, after 3, 6, 12 and 24 weeks and thereafter when clinically needed

– DHPC in October 2012
– DHPC in September 2013
– aRMM in November 2014 (Physician's guide to prescribing, including a liver monitoring scheme, and the Patient's Booklet)

HOW?

- Prescription Centre of EHIF - all agomelatine prescriptions of new users during 01.01.2012-31.05.2016

  New users - patients who had not been prescribed agomelatine during 2011

  Only purchased prescriptions were included

  Patients without health insurance were excluded (non-insured patients are charged for tests)

HOW?

- EHIF Information System - all liver function tests of these patients

  The code field contains AST, ALT, plus ALP, LDH, CPK, GGT, CPK-Mba, Alpha-amylase

  Consequently the result may be slightly more positive of the actual situation

  Whether tests were performed initiating and during treatment:

- compared the test date with period of 15 days or 30 days before first purchase;
- compared the test date with period of +/-15 days or +/-30 days from each purchase;

WHAT?

- 5 630 new users started with agomelatine (17 377 prescriptions)
- Mainly prescribed by psychiatrists (55%) and by GP's (39%)
- Most commonly prescribed for depression (31%), anxiety disorders (21%) and recurrent depressive disorders (17%)
- Patients age range - 4-96 years (! Indicated 18-75 years)
  - 0.6% (35) were children and adolescent <18 years
  - 6.4% (363) were ≥75 years

WHAT?

- An average of 3,1 prescriptions per patient and 1,3 packages per prescription - average of 4 months treatment (median 2 months)

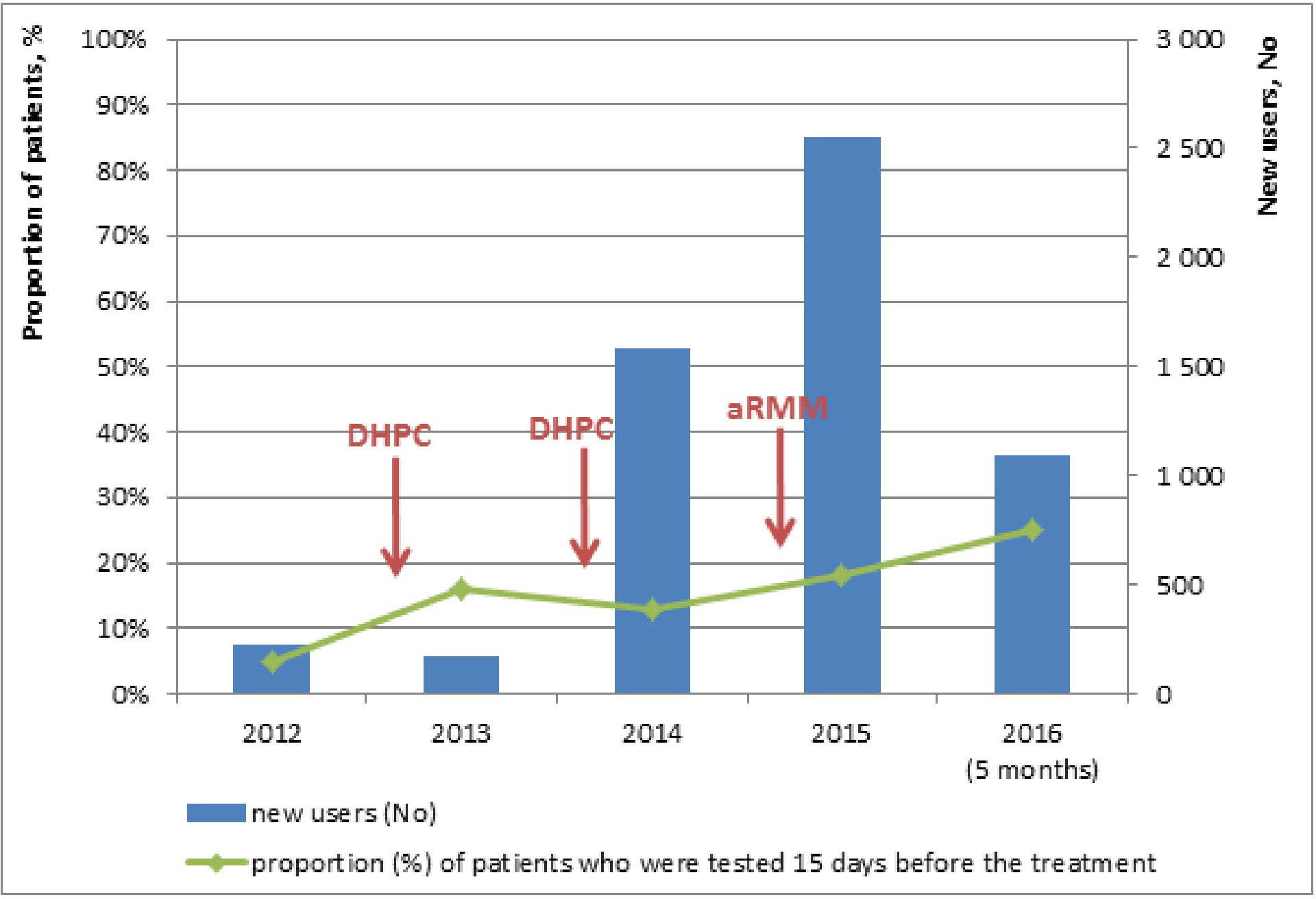
- During the study period the patients had been tested 19 026 times, an average 3.8 tests per patient

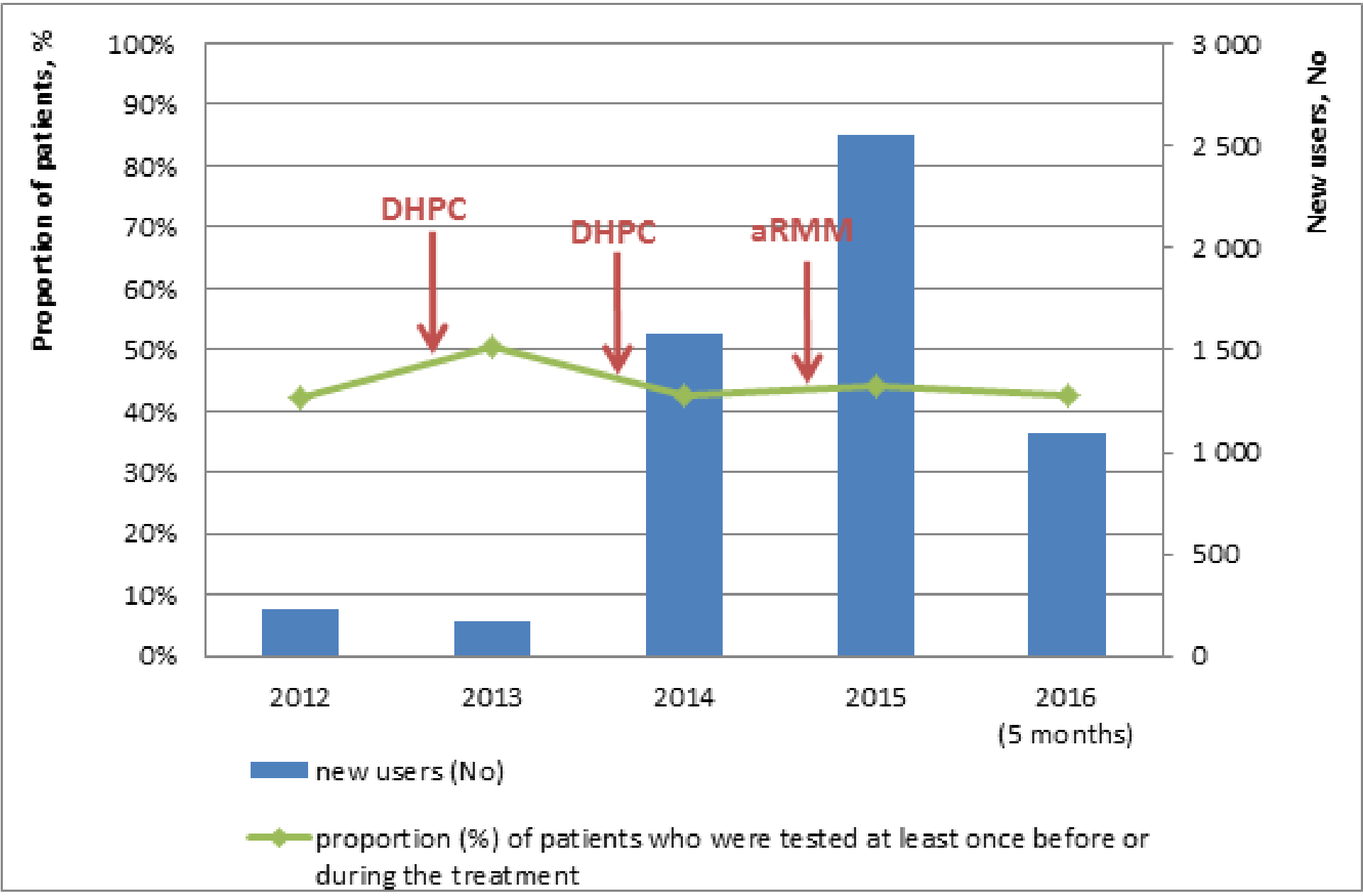
WHAT?

- Monitoring of LF at the initiation of treatment
  - In 17% (984) the test was performed 15 days before starting the treatment,
    - 23% in children and adolescent
    - 12% in elderly (≥75 years).
  - Extending the period to 30 days before treatment in 23% (1 267) of patients the test was performed,
    - 23% in children and adolescent
    - 17% in elderly (≥75 years).
  - 54% of the cases the tests were ordinated by general practitioner, 35% by psychiatrist.

WHAT?

- Monitoring of LF during the treatment:
  - In 37% (2 094) of patients at least one test was performed during treatment in +/- 15 days of prescription purchase.
  - Extending the period to +/- 30 days - in 45% (2 560) of patients at least one test was performed during treatment.
  - 1 029 (18%) patients received agomelatine at least for 6 months,
    - In 66% (684) at least one test was performed during treatment
    - In 4% (42) tests were performed according to the liver monitoring scheme


Proportion of patients, %
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
3 000
2 500
2 000
1 500
1 000
500
0
New users, No
DHPC
DHPC
aRMM
2012
2013
2014
2015
2016
(5 months)
new users (No)
proportion (%) of patients who were tested 15 days before the treatment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New users, No
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2012
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2014
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2016
(5 months)
new users (No)
proportion (%) of patients who were tested at least once before or during the treatment

SO?

As regards study results:

- Adherence to the liver monitoring scheme is poor.
- Further regulatory action / communication is essential

SO?

As regards study methods - CONS

- data it is not always marker specific (billing data is based on health care services - many markers may be coded in one code field)
- it is not possible to inquire test results
- defining the feasibility of study characteristics with EHIF is challenging

SO?

As regards study methods – PROS

EHIF database contains data of prescriptions and reimbursed Hcare services (using patient's ID-code lab tests, procedures, diagnosis can be linked)

EHIF data can be used to investigate

- what medicines are used together
- what tests/procedures are done prior/during/after T
- in which indication and population the medicine is used (contraindication, off-label use)
- are prescribing and dispensing restrictions followed (limited amount of medicine per prescription, dispensing time)

SO?

As regards study methods – when can be used?

Examples of future investigations may be:

- Valproate use and switching to an alternative treatment when patient becomes pregnant
- Combined use of medicines affecting the RAS - use of aliskiren, AKE inhibitors and ARBs (trends over time)
- Isotretinoin and medically supervised pregnancy testing prior treatment /before every prescription, length of the prescription (1 month) in fertile women

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Thank you!

Any questions ?

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