SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale della Romagna

La sorveglianza epidemiologica dello screening dei tumori del collo dell'utero nella Regione Emilia-Romagna

14 Marzo 2016

Tavola rotonda: promozione della qualità nel programma di screening cervicale.

Concordanza sul test HPV

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Commercially available molecular tests for human papillomaviruses (HPV): 2015 update

Journal of Clinical Virology 76 (2016) S3–S13

Mario Poljak*, Boštjan J. Kocjan, Anja Oštrbenk, Katja Seme

Table 1
hr-HPV DNA screening tests present on the market in August 2015.

Tests targeting IARC-2009 hr-HPV types plus HPV66 and/or HPV68
Hybrid Capture 2 (HC2) HPV DNA Test (Qiagen Gaithersburg, Inc., MD, USA)
EIA kit HPV GP HR (Diassay, Ev Rijswijk, The Netherlands)
Cervista HPV HR Test (Hologic, Madison, WI, USA)
CareHPV Test (Qiagen Gaithersburg, Inc., MD, USA)
Amplicor HPV Test (Roche Molecular Systems Inc., Alameda, CA, USA)
13 High-risk HPV Real-time PCR Kit (Hybribio, Beijing, China)
Biorad Dx HR-HPV Auto Assay (Bio-Rad, Hercules, CA, USA)
Tests targeting IARC-2009 hr-HPV types only
HPV High Risk Screen Real-TM Quant (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
HPV High Risk Screen Real-TM Quant 2 x (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
AmpliSens HPV HCR screen-titre-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic) and 1 variant
Tests targeting IARC-2009 hr-HPV types and additional alpha-HPV types
HPV-Risk assay (Self-Screen BV, Amsterdam, The Netherlands)
Seeplex HPV4A ACE Screening (Seegene, Seoul, Korea)
Urine-Based HPV (High and Low Risk) PCR Detection Kit (Norgen, Thorold, Canada)
STD Kit (Autoimmun Diagnostika GmbH, Strassberg, Germany)
AmpliSens HPV HCR screen-Eph PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic) and 1 variant
HPV-DNA Assay Kit (Tofema, Seoul, Korea)
PapilloScreen (GeneMatrix Co., Seoul, Korea)
HPV Screen PCR Kit (BioCore, Seoul, Korea)
AmpliQuality HPV-SM (AB Analitica, Padova, Italy)
AmpliQuality HPV-HS Bio (AB Analitica, Padova, Italy)
Human Papilloma Virus (HPV Common/double check) (Genekam Biotechnology, Duisburg, Germany)
BIOPAP Kit (Biotools, Nave, Spain)
High-risk human papillomavirus DNA Diagnostic kit (Sansure Biotech Inc., Changsha, Hunan, China)
Tests targeting a subset of IARC-2009 hr-HPV types
HPV High Risk Screen (Sacace, Como, Italy; Nuclear Laser Medicine S.R.L., Milano, Italy)
AmpliSens HPV HCR screen-FEP PCR kit (3x) (Federal State Institution of Science, Moscow, Russia; Ecoli, Bratislava, Slovak Republic)
HPV Total & High Risk (Clonit, Milano, Italy)
Absolute HPV HR Test (BioSewoom, Seoul, Korea)
HPV Screening (Clonit, Milano, Italy)
Cancer Molecular Marker TEST (GoodGene, Seoul, Korea)

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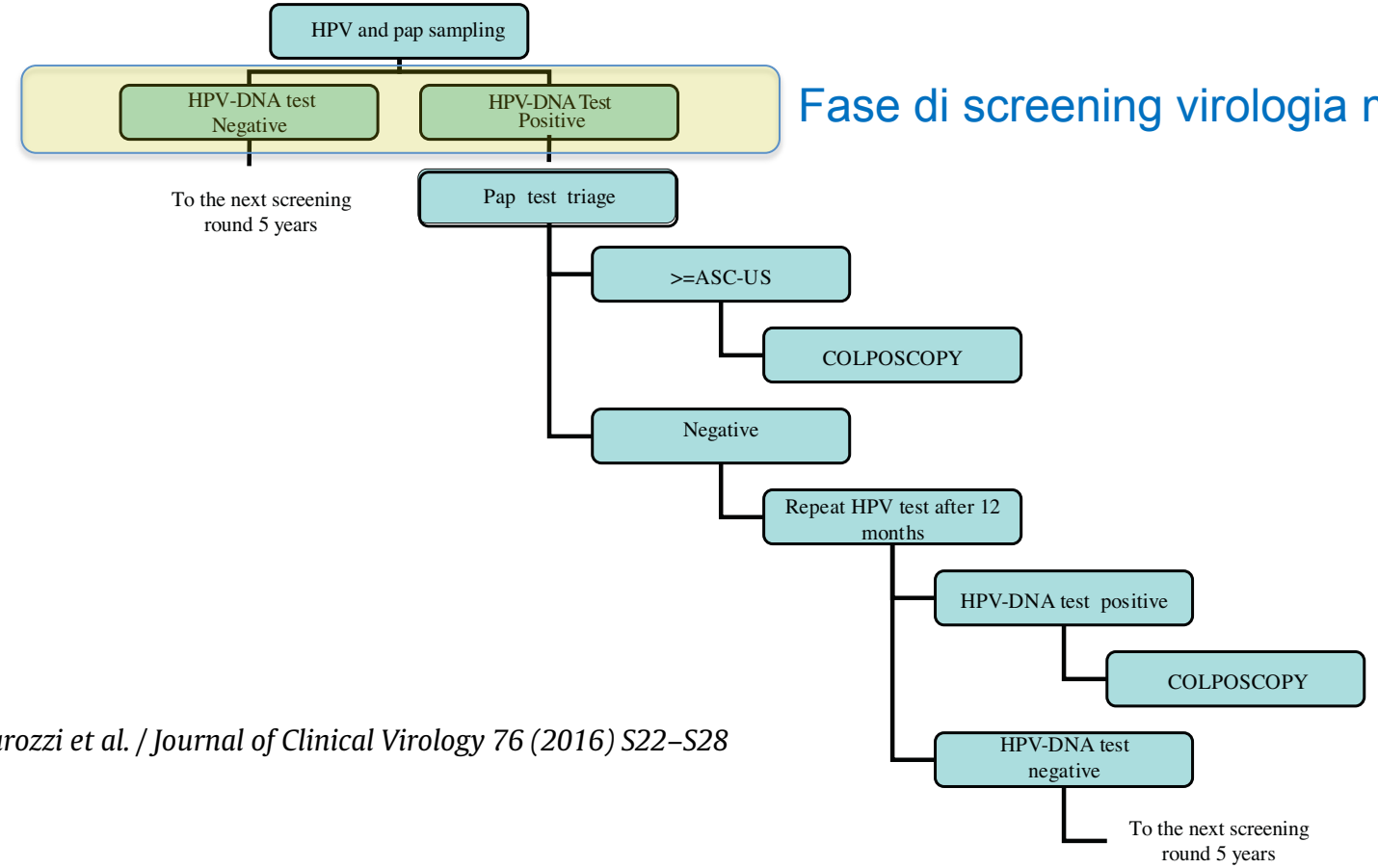
With such an exceptionally high number of commercial HPV tests on the market, alpha-HPVs are currently still among most attractive microbial targets for molecular diagnostic companies.

Unfortunately, today's HPV test global market is one of the most confusing and least regulated, and with most divergent diagnostic products on the market, sometimes colloquially described as the "Wild West."

In addition, we can predict with high certainty that the number and diversity of commercial HPV tests will *continue to increase* over the next 5 years due to the promising marketing opportunities for manufacturers around the world.

110/193 (57.0%) of HPV tests on the market in 2015 had at least one publication in peer-reviewed literature as of August 31, 2015. However, only 69/193 (35.7%) of HPV tests on the market in 2015 had a documented performance evaluation (analytical and/or clinical) in peer-reviewed literature as of August 31, 2015 in contrast to the remaining 41 HPV tests, for which only descriptive studies can be found in the literature.

EQA e ICQ: garantiscono la fase del processo relative alla virologia



Fase di screening virologia molecolare

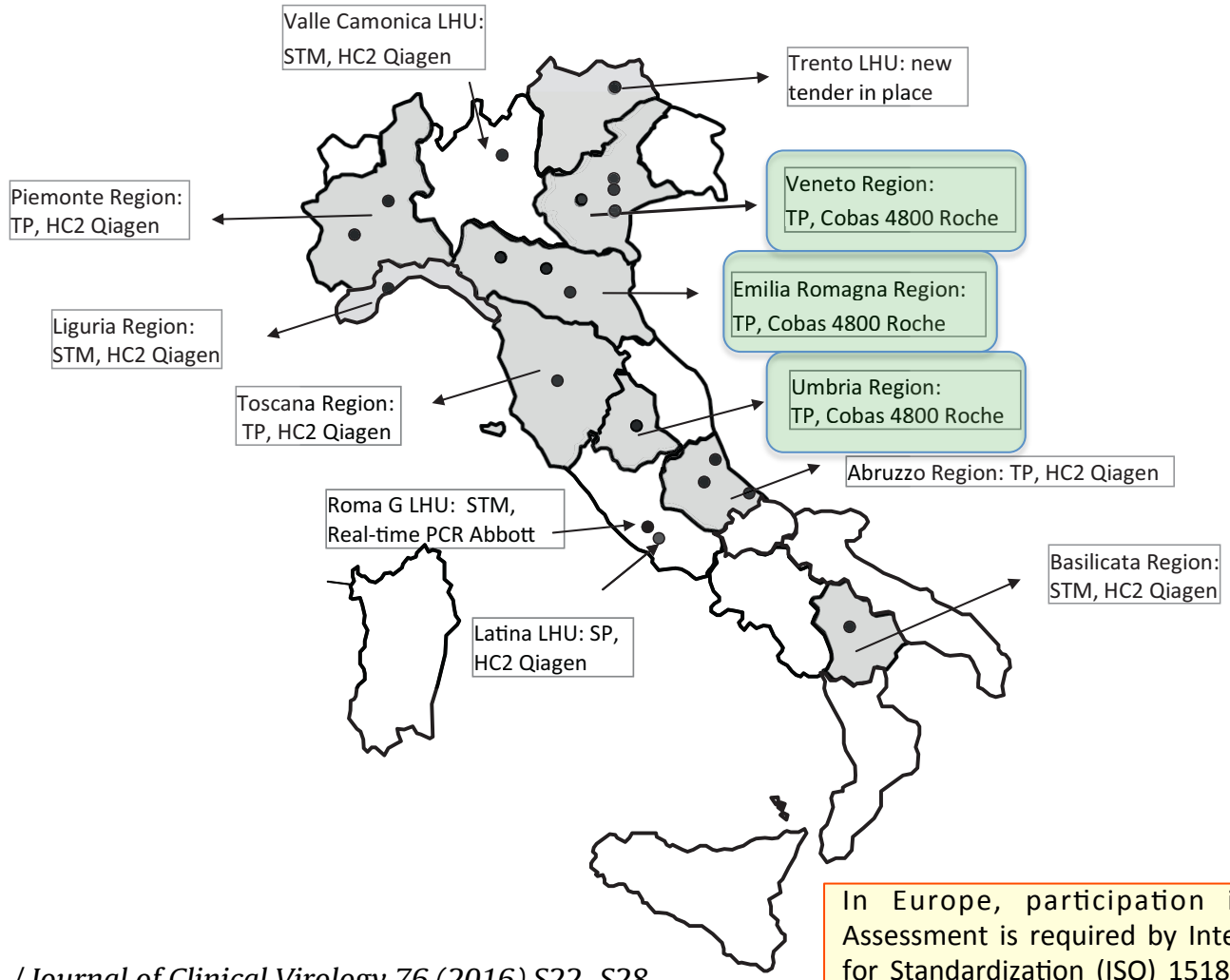
F.M. Carozzi et al. / Journal of Clinical Virology 76 (2016) S22–S28

Controllo di Qualità

- Controllo Interno (IQC)
  - DIVERSO DA K del kit
  - POSSIBILMENTE “INDIPENDENTE”
  - MATERIALE BIOLOGICO MONODONATORE
  - VARIAZIONI INTRALAB E INTERLAB “A BREVE”
  - OPEN QUESTIONS:
    - Frequenza?
    - Materiali?
    - Modalità?
    - Networking INTRA e/o INTER regione

Controllo di Qualità

- Valutazione Esterna di Qualità (EQA)
  - PROGRAMMI DA TERZE PARTI
  - POSSIBILMENTE “INDIPENDENTE”
  - MATERIALE BIOLOGICO MONODONATORE
  - ACCURATEZZA DEL SINGOLO VERSUS NETWORK “OVER TIME”
  - OPEN QUESTIONS:
    - LOD?
    - Materiali? Fasi del processo?
    - Variazioni fra metodi analitici?
    - Networking internazionale



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In Europe, participation in External Quality Assessment is required by International Organization for Standardization (ISO) 15189:2007 and by specific National Accreditation rules

HPV testing for primary cervical screening: Laboratory issues and evolving requirements for robust quality assurance

Francesca Maria Carozzi[a,*], Annarosa Del Mistro[b], Kate Cuschieri[c], Helena Frayle[b], Cristina Sani[a], Elena Burroni[a]

Journal of Clinical Virology 76 (2016) S22–S28

….. usually in clinical virology it is important to use methods with the highest sensitivity for the micro-organism to diagnose the infection. [OR WELL CALIBRATED SAMPLES FOR VIRAL LOADS]

The 'hrHPV test' applied to the screening program does not follow this rule; it is a test for ***oncogenic risk*** because the aim of the screening program is to identify women with or at risk of cervical precancerous lesions.

……the test must be optimized for a pre-specified clinical sensitivity and specificity, according to the international guidelines keep in mind that the cut-off used in this context does not correspond to the minimum detectable level of the assay.

…….we need HPV EQA programs specific for HPV-based screening, optimized to evaluate clinical performance, and applicable to different assays and different collection media.

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HPV EQA, examples of available programs.

EQA program	Peculiarities	Advantages	Disadvantages
UK NEQAS	- Pooled material of clinical origin, in ThinPrep medium - 4 specimens, 3 times a year - HR HPV types - Scores on qualitative performance	- Samples representative of clinical specimens - Evaluation of all processing steps - Periodic evaluation	- No choice of medium - Results not elaborated taking into account semi-quantitative data
QCMD	- Cell line material and clinical samples - 8-10 specimens, in ThinPrep - HR types - Two kinds of samples: core and educational - Score assigned on core results	- Samples representative of clinical specimens - Evaluation of all processing steps - Clinical evaluation	- Annual panel, only one evaluation/year - No choice of medium - Missed untargeted HPV types scored as error
DicoCare	- Lyophilized clinical samples, to be resuspended in the medium in use - 8 specimens, shipped together, to be tested 2×4 times a year - HR HPV types	- Samples representative of clinical specimens - Evaluation of all processing steps - Choice of medium - Periodic evaluation	- Medium re-suspension may affect the final results and the comparison between labs
WHO HPV LabNet	- 46 specimens; 43 plasmid-based + 3 cell lines-based, in phosphate buffer - HR and 2 LR HPV types	- Stable material - Representative of most significant HPV types	- Mainly synthetic DNA samples -Designed for typing evaluation - High sensitivity - Annual panel, only one evaluation/year -Medium not representative of media used
Instand	- 10 specimens in two shipments - Lyophilized clinical samples, to be resuspended in the medium in use - HR and LR HPV types	- Samples representative of clinical specimens - Evaluation of all processing steps - Choice of medium - Periodic evaluation	- Medium re-suspension may affect the final results and the comparison between labs

Riunione del TT regionale dell'HPV-test

Bologna, 26.02.2016

ICQ-EQA: piano per il 2016: viene condivisa la necessità di procedere alla stesura di un protocollo comune che stabilisca le modalità e la tempistica d'uso dei controlli interni.

Viene altresì condivisa l'opportunità di formalizzare un controllo di qualità dei test biomolecolari attraverso il sistema *Neqas* (proposto dalla Ditta *Roche*) e, almeno per un primo periodo, con un sistema esterno alla fornitura di gara (*Instand e.V.*, Dusseldorf).

Sono peraltro in corso attività presso le Regioni e il GISCi, per formalizzare un protocollo nazionale VEQ che sarà verosimilmente assunto non appena disponibile.

Sono in corso di valutazione possibili sinergie di ICQ con altre Regioni