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Review

Meeting report: 26th International Conference on Antiviral Research [☆]

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ABSTRACT

The 26th International Conference on Antiviral Research (ICAR) was held in San Francisco, California from May 11 to 15, 2013. This article summarizes the principal invited lectures at the meeting. The opening symposium on the legacy of the late Antonín Holý included presentations on his pioneering work with nucleotide analogs, which led to the development of several antiviral drugs including tenofovir. This drug has transformed the treatment of HIV infection and has recently become the first-line therapy for chronic hepatitis B. The Gertrude Elion Award lecturer described the anti-HIV activities of the CCR5 inhibitor cenicriviroc and the reverse transcriptase inhibitor festinavir[®], and also reviewed the evaluation of biodegradable nanoparticles with adjuvant activity. The William Prusoff Award winner reported on the creation of NAOMI, a computer model with 21 enzymes to predict the activity of nucleoside analogs against hepatitis C virus (HCV). Other invited lecturers discussed the development of countermeasures against severe dengue and the potential of RNA virus capping and repair enzymes as drug targets. Topics in the clinical symposium included the current status of the anti-HCV compounds sovalprevir, ACH-3102, miravirsin and ALS-2200; the evaluation of single-tablet regimens for HIV infection; and the investigation of cytomegalovirus resistance to CMX001. Two chemistry minisymposia examined strategies and tactics in drug design and the use of prodrugs as a successful approach in drug discovery.

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65 7.4. Cenicriviroc, a novel, once-daily, potent dual CCR5 and CCR2 antagonist under investigation for treatment of HIV infection. 00
 66 7.5. The STaR study: single tablet regimen rilpivirine/emtricitabine/tenofovir DF is non-inferior to efavirenz/emtricitabine/tenofovir DF in ART-
 67 naïve adults. 00
 68 7.6. CMV resistance profile of CMX001. 00
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76 **1. Introduction**

77 This article provides a summary of the invited lectures at the
 78 26th International Conference on Antiviral Research, sponsored
 79 by the International Society for Antiviral Research (ISAR), which
 80 was held in San Francisco, California from May 11 to 15, 2013.
 81 The report begins with a synopsis of the symposium held in mem-
 82 ory of the late Antonín (Tony) Holý, followed by brief summaries of
 83 lectures by the recipients of ISAR’s two major awards, the keynote
 84 address, the plenary lecture, the clinical symposium, and the two
 85 chemistry minisymposia. Because this paper simply provides over-
 86 views of oral presentations, it is not accompanied by references to
 87 the scientific literature. Any descriptions of favorable treatment
 88 outcomes should not be taken as a recommendations for clinical
 89 use.

90 **2. The legacy of Antonín (Tony) Holý: Nucleotides in the**
 91 **treatment and prevention of chronic viral infections**

92 *2.1. A personal note on the contribution and legacy of Tony Holý*

93 Erik De Clercq, Rega Institute for Medical Research, Leuven, Bel-
 94 gium (Fig. 1A).

95 Erik described his first meeting with Tony Holý at a symposium
 96 on Synthesis of Nucleosides, Nucleotides and Polynucleotides, 3–5
 97 May 1976 in Göttingen, Germany. He felt out of place, but privi-
 98 leged to be the only MD present among so many PhD chemists.
 99 Similarly, Erik found himself with many chemists at the NATO
 100 meetings in 1979 and 1983. The meeting, at Il Ciocco, Italy in
 101 May 1987, can be regarded as a model for ICAR meetings. (A pho-
 102 tograph of the attendees at this meeting was included in the ISAR
 103 News 22-1). Tony Holý became a regular attendee at ICAR
 104 meetings.

105 Tony’s first clinical success was Duvira® gel which was licensed
 106 in Czechoslovakia for herpes labialis (see John Martin’s presenta-
 107 tion below). The phosphonate compound, (S)-HPMPA, was too

108 toxic for progression to clinical use but it was the first of a long ser-
 109 ies of compounds. Cidofovir (HPMPC) is used to treat herpesvirus
 110 infections, mainly cytomegalovirus (CMV), when a resistance to
 111 first-line therapy occurs. Adefovir dipivoxil (ADV) was licensed to
 112 treat hepatitis B. But there is one drug which stands out as being
 113 exceptional. Tenofovir, as its oral prodrug, was approved for HIV
 114 therapy in 2001 and, in combination with emtricitabine (FTC) as
 115 Truvada, was approved in 2004. Atripla (combination of truvada
 116 and efavirenz) was approved in 2006. Complera (in USA) [and
 117 Eviplera (in Europe)] was approved in 2011, and the “Quad pill”
 118 Stribild (containing truvada, elvitegravir and cobicistat) was ap-
 119 proved in 2012 (in USA) and 2013 (in Europe). These single-tablet
 120 regimens, all of which contain tenofovir as a key component, have
 121 transformed HIV therapy and are giving patients many years of
 122 near-normal life.

123 When visiting Tony at Olomouc, Czechoslovakia, Erik noticed a
 124 UNESCO-classified monument dedicated to “The Holy Trinity”.
 125 That stimulated Erik’s thinking. He was one of a team, Tony Holý
 126 the chemist, Erik the MD and John Martin (also a chemist) from Gi-
 127 lead. It was the long and close collaboration among these three
 128 which enabled tenofovir to become a life-saving therapy. It seemed
 129 as if Erik and John were part of a different trinity, “a Holý trinity”.
 130 Erik showed several photographs of this “Holý trinity” in various
 131 exotic locations including the Rio Grande Gorge (New Mexico) in
 132 1995 when the ICAR meeting was at Santa Fe (Fig. 2).

133 In 2003, John Martin presented Tony and Erik with a plaque of
 134 recognition by Gilead Sciences. In 2008, there was a campaign pro-
 135 moting Czech successes and Tony featured in a display at Prague
 136 airport (now called Vaclav Havel airport) – Tony was considered
 137 as the leading scientist of the Czech Republic. Truvada was ap-
 138 proved for prophylactic use, to prevent the spread of HIV, on the
 139 very day that Tony died. (16 July 2012).

140 *2.2. A tribute to Antonín Holý*

141 John Martin, Gilead Sciences, Foster City, CA, USA (Fig. 1B)



Fig. 1. Legacy of Tony Holý: Erik De Clercq (left) and John Martin (right) giving their tributes.

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