

## Cancer

# Management of AIDS-Related Kaposi Sarcoma: Advances in Target Discovery and Treatment

Bruce J. Dezube, MD; Liron Pantanowitz, MD; David M. Aboulafia, MD

*Kaposi sarcoma (KS) is the most common tumor arising in HIV-infected patients and is considered an AIDS-defining illness by CDC guidelines. Recent advances in the elucidation of the pathogenesis of KS continue to uncover potential targets for therapies. Such targets include the KS herpesvirus/human herpesvirus 8 and the processes of angiogenesis and cellular differentiation. Five agents are currently approved by the FDA for the treatment of KS: alitretinoin gel for topical administration and liposomal daunorubicin, liposomal doxorubicin, paclitaxel, and interferon- $\alpha$  for systemic administration. Many more agents, particularly angiogenesis inhibitors and other pathogenesis-targeted therapies, are in clinical development. With increasing recognition that effective antiretroviral regimens are associated with both a decreased proportion of new AIDS-defining KS cases and a regression in the size and number of existing KS lesions, most, if not all, patients with KS should be advised to take antiretroviral drugs that will maximally decrease HIV-1 RNA levels. [AIDS Reader. 2004;14:000-000]*

**Key words:** HIV / AIDS • Cancer • Kaposi sarcoma • Human herpesvirus

**K**aposi sarcoma (KS) is the most common tumor arising in HIV-infected patients and is considered an AIDS-defining illness according to CDC guidelines. In the United States, KS is over 20,000 times more common in persons with AIDS than in the general population and over 300 times more common than in other immunosuppressed patients, such as renal transplant recipients.

A basic knowledge of the pathogenesis of AIDS-related KS is important for understanding the possible targets for KS therapies. Recent research has provided tremendous insight into how the KS herpesvirus/human herpesvirus 8 (KSHV/HHV-8) creates the inflammatory-angiogenic milieu necessary for the growth of this tumor.

## **PATHOGENESIS AND POTENTIAL THERAPEUTIC TARGETS**

The pathogenesis of AIDS-related KS is multifactorial and involves KSHV/HHV-8, altered expression and response to cytokines, and stimulation of KS growth by the HIV-1 transactivating protein Tat, as well as other factors yet to be described.<sup>1</sup> KSHV/HHV-8 is a gamma herpesvirus that is a necessary, but not sufficient, cause of KS (Figure 1). KSHV/HHV-8 encodes viral proteins that are homologues of human interleukin (IL)-6, chemokines of the macrophage inflammatory protein family, cell cycle regulators of the cyclin family, and anti-apoptosis genes of the bcl-2 family.

Tat promotes the growth of KS lesional spindle cells of lymphatic endothelial origin (Figure 2) but does

so only in the presence of inflammatory cytokines.<sup>2,3</sup> The synergy between cytokines and the HIV-1 Tat protein, as well as the immunosuppression associated with AIDS, suggests a basis whereby AIDS-related KS is more aggressive than the classic form of KS, in which the HIV-1 Tat protein does not play a role.

The creation of an inflammatory-angiogenic state by KSHV/HHV-8 may be the critical step in the pathogenesis of KS.<sup>4</sup> The remarkable finding that KSHV/HHV-8 encodes viral IL-6 and that IL-6, in turn, leads to expression of vascular endothelial growth factor (VEGF)<sup>5</sup> provides a missing link in the chain of events by which KSHV/HHV-8 creates an inflammatory-angiogenic environment. Furthermore, the G protein-coupled receptor oncogene of KSHV/HHV-8 activates the VEGF receptor-2 (KDR), important to the angiogenic process.<sup>6</sup>

KS lesions may undergo spontaneous or treatment-related regression. Regression, characterized by an absence of detectable lesional spindle cells, is accompanied by a decrease in KSHV/HHV-8 and cyclin-D1 expression.<sup>7</sup>

## **CLINICAL FEATURES**

### **Cutaneous Involvement**

AIDS-related KS has a highly variable clinical course, ranging from minimal disease presenting as an incidental finding to explosive growth resulting in significant morbidity and mortality. The skin lesions appear most often on the lower extremities, face (especially the nose), and genitalia.<sup>8</sup> The colors associated with these lesions include many hues of

*Dr Dezube is director of the AIDS Malignancy Research and Treatment Center at the Beth Israel Deaconess Medical Center and associate professor of medicine at Harvard Medical School, Boston. Dr Pantanowitz is a hematopathology fellow at the Beth Israel Deaconess Medical Center and Harvard Medical School. Dr Aboulafia is attending hematologist/oncologist at the Virginia Mason Medical Center, Seattle.*

# Recent Advances In Aids And Kaposi Sarcoma

**Martin C. Woodle, Gerrit Storm**



## **Recent Advances In Aids And Kaposi Sarcoma:**

*Immunobiology of Proteins and Peptides VI* M.Zouhair Atassi,1992-01-31 The articles in this volume represent papers delivered by invited speakers at the 6th International Symposium on the Immunobiology of Proteins and Peptides In addition a few of the abstracts submitted by participants were scheduled for minisymposia and some of the authors whose presentations were judged by the Scientific Council to be of high quality were invited to submit papers for publication in this volume This symposium was established in 1976 for the purpose of bringing together once every two or three years active investigators in the forefront of contemporary immunology to present their findings and discuss their significance in the light of current concepts and to identify important new directions of investigation The founding of the symposium was stimulated by the achievement of major breakthroughs in the understanding of the immune recognition of proteins and peptides We believed that these breakthroughs will lead to the creation of a new generation of peptide reagents which should have enormous potential in biological therapeutic and basic applications This anticipated explosion has in fact since occurred and many applications of these peptides are now being realized

*Recent Advances in Mucosal Immunology* Jiri Mestecky, Jerry R. McGhee, John Bienenstock, Pearay L. Ogra, 2012-12-06 Increasing interest in the immunology of mucosal surfaces is obvious from the number of publications in scientific journals and from the frequency of national and international symposia devoted to this subject Particularly encouraging are the large numbers of young investigators who have chosen to work in this area of theoretical immunology with profound practical implications The two volumes represented here are the result of an International Congress Of Mucosal Immunology held at the Niagara Falls Convention Center and the Niagara Falls Hilton on June 29 July 3 1986 This satellite meeting of the International Congress of Immunology placed emphasis on all aspects of the Mucosal Immune System This included the regulation of differentiation of mucosal lymphocytes mucosa associated lymphoreticular tissue and lymphocyte homing the immunology of mucosa associated tissues and glands effector functions in mucosal immunity and the effects of environmental antigens on the immune response all of which are included in Volume I The second volume has emphasized studies of the immune response and effector functions IgA biosynthesis and transport IgA proteases and effector functions developmental aspects and immunodeficiency the immunopathology of IgA and mucosal immunoprophylaxis A total of 218 papers are included in these two volumes and a comparison to past meetings held at four to five year intervals indicates the explosive growth of mucosal immunology

*Disease Control Priorities, Third Edition (Volume 6)* King K. Holmes, Stefano Bertozzi, Barry R. Bloom, Prabhat Jha, 2017-11-06 Infectious diseases are the leading cause of death globally particularly among children and young adults The spread of new pathogens and the threat of antimicrobial resistance pose particular challenges in combating these diseases Major Infectious Diseases identifies feasible cost effective packages of interventions and strategies across delivery platforms to prevent and treat HIV AIDS other sexually transmitted infections tuberculosis malaria adult febrile illness viral hepatitis and neglected tropical diseases The volume

emphasizes the need to effectively address emerging antimicrobial resistance strengthen health systems and increase access to care The attainable goals are to reduce incidence develop innovative approaches and optimize existing tools in resource constrained settings Current Catalog National Library of Medicine (U.S.), First multi year cumulation covers six years 1965 70 Recent Advances in AIDS and Kaposi's Sarcoma ,1987 *HIV/AIDS-Associated Viral Oncogenesis* Craig Meyers,2018-12-06 One of the most important aspects of AIDS is the loss of protective immune function in the infected host which leads to increased prevalence of opportunistic infections and cancers This book specifically addresses viral induced human cancers associated with AIDS and observed in the AIDS population It addresses the specific treatment required in this special population and the molecular biology of the causative viral agents , **New Drug Development for Known and Emerging Viruses** Helga Rübsamen-Schaeff,Helmut Buschmann,2022-01-31 Discusses how to fight Ebola SARS Corona and other known or emerging human viruses by building on the successes in antiviral therapy of the past decades Written by leading medicinal chemists from academia and industry this book discusses the entire field of antiviral drug discovery and development from a medicinal chemistry perspective focusing on antiviral drugs targets and viral disease mechanisms It provides an outlook on emerging pathogens such as Ebola Zika West Nile Lassa and includes a chapter on SARS Coronaviruses 2 causing the present pandemic New Drug Development for Known and Emerging Viruses describes the discovery and development process for antiviral agents for different classes of viruses and targets based on the experiences from the nine human viruses for which approved drugs are on the market HIV HCV Influenza RSV HBV HPV HCMV HSV and VZV It covers the properties and potential of 20 classes of currently approved antivirals including combination drugs and looks at novel antiviral strategies against emerging viruses Covers the entire field of antiviral drug discovery and development Addresses the need for antiviral drugs to combat major health threats such as Ebola Zika West Nile and SARS Coronavirus 2 Summarizes the successes of the past 15 years in developing ground breaking medicines against 9 major human viruses both from the medicinal chemistry and the pharmacological angle Discusses practical and strategic challenges in the drug discovery and development process including screening technologies latency and toxicity issues New Developments in Antiviral Drugs is an important book for medicinal chemists pharmaceutical chemists virologists and epidemiologists and will be of great interest to those in the pharmaceutical industry and public health agencies

Cutaneous Manifestations of HIV Disease Clay Cockerell,Antoanella Calame,2012-10-14 Dermatologists are often the first medical professionals to see patients with HIV infection as skin diseases are common in acquired immunodeficiency syndrome This book aims to help dermatologists recognize the cutaneous manifestations of HIV infection and AIDS so that diagnosis can be made quickly and therapy begun as soon as possible The book HIV and the New Viruses Angus G. Dalgleish,Robin A. Weiss,1999-03-16 HIV and the New Viruses presents cutting edge reviews of persistent human virus infections as a coherent collection for the first time These cover recently discovered viruses such as HHV 6 HHV 8 and HCV

as well as the latest research on HIV This comprehensive and updated reference includes an in depth study of the major issues in the epidemiology pathogenicity molecular virology host responses and management of conditions associated with those viruses Information on new pharmaceuticals and vaccine developments is also included Edited by the leading experts in the field HIV and the New Viruses will be essential reading for postgraduates clinicians and researchers in virology immunology cancer molecular biology and the pharmaceutical industry Presents cutting edge reviews of persistent human virus infections as a coherent collection for the first time Includes an in depth study of the major issues in the epidemiology pathogenicity molecular virology host responses and management of conditions associated with those viruses **Long**

**Circulating Liposomes: Old Drugs, New Therapeutics** Martin C. Woodle, Gerrit Storm, 2013-06-29 This book provides an up to date evaluation of clinical aspects of newly available long circulating liposome formulations Based on results from numerous clinical studies the book describes the fundamentals of this new technology discusses how it may influence the pharmacology of existing well known agents reformulated in this manner and elaborates on future expectations It provides the practicing clinician in particular oncologists and critical care infectious disease physicians with the tools needed to use these new formulations towards the best outcome for the patient **Recent Advances in Ophthalmology-12** HV

Nema, Nitin Nema, 2015-05-10 Recent Advances in Ophthalmology 12 is the latest volume of this collection of reviews of the most recent developments in the field of ophthalmology The book consists of sixteen chapters Recent advances covered include the use of femtosecond laser in cataract surgery the diagnosis and management of ocular AIDS chapters on enhanced depth imaging technology OCT and the use of intravitreal avastin Other topics include the present status of phakic IOLs the future of LASIK refractive surgery for the treatment of myopia hypermetropia and astigmatism and the latest developments in the treatment of glaucoma This comprehensive update of ophthalmology topics with over 100 full colour images and illustrations is an essential resource for postgraduates and residents in ophthalmology ophthalmic practitioners and ophthalmic consultants Key Points Latest volume in the Recent Advances in Ophthalmology series Over 100 full colour images and illustrations Previous volume published 2013 Journal of the National Cancer Institute , 2002 **Recent**

**Advances in Sexually Transmitted Diseases** John R. Harris, 1991 An examination of recent research into sexually transmitted diseases Topics covered include the gastrointestinal manifestations of HIV 1 infection heterosexual transmission of the HIV infection and HTLV I HTLV II and HTLV III related neoplasms **Advances in Virus Research** , 2010-11-25 Published since 1953 Advances in Virus Research covers a diverse range of in depth reviews providing a valuable overview of the current field of virology The impact factor for 2008 is 4.886 placing it 4th in the highly competitive category of virology Contributions from leading authorities Informs and updates on all the latest developments in the field National Library of Medicine Current Catalog National Library of Medicine (U.S.), **New Insights into HIV/AIDS for Students and**

**Healthcare Professionals** Esther Olufunmilayo Asekun-Olarinmoye, Olutayo Christopher Alebiosu, 2019-01-24 Since the first

case of HIV was diagnosed in 1981 several efforts have gone into its prevention and control However it remains a leading scourge today with no cure despite the international attention and publicity it receives It is one of the few diseases specifically given attention in the Millennium Development Goals MDG and the Sustainable Development Goals SDGs There has been inadequate effort by academia in developing countries towards contributing to in depth knowledge of HIV as well as stimulating the interest of students in the topic As the search for a cure continues this book is timely discussing the changing epidemiology of HIV The contributors are not only academicians but also seasoned programmers who are working in the realm of HIV care     **Recent Advances in AIDS and Kaposi's Sarcoma** G. Giraldo,E. Beth-Giraldo,G. Castello,M.

Pergola,D. Zarrilli,1987-07-08

Cumulated Index Medicus ,1993

*HIV/AIDS Surveillance* ,1994

## Reviewing **Recent Advances In Aids And Kaposi Sarcoma**: Unlocking the Spellbinding Force of Linguistics

In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is actually astonishing. Within the pages of "**Recent Advances In Aids And Kaposi Sarcoma**," an enthralling opus penned by a highly acclaimed wordsmith, readers set about an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve in to the book is central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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### **Table of Contents Recent Advances In Aids And Kaposi Sarcoma**

1. Understanding the eBook Recent Advances In Aids And Kaposi Sarcoma
  - The Rise of Digital Reading Recent Advances In Aids And Kaposi Sarcoma
  - Advantages of eBooks Over Traditional Books
2. Identifying Recent Advances In Aids And Kaposi Sarcoma
  - Exploring Different Genres
  - Considering Fiction vs. Non-Fiction
  - Determining Your Reading Goals
3. Choosing the Right eBook Platform
  - Popular eBook Platforms
  - Features to Look for in an Recent Advances In Aids And Kaposi Sarcoma
  - User-Friendly Interface
4. Exploring eBook Recommendations from Recent Advances In Aids And Kaposi Sarcoma
  - Personalized Recommendations
  - Recent Advances In Aids And Kaposi Sarcoma User Reviews and Ratings
  - Recent Advances In Aids And Kaposi Sarcoma and Bestseller Lists

5. Accessing Recent Advances In Aids And Kaposi Sarcoma Free and Paid eBooks
  - Recent Advances In Aids And Kaposi Sarcoma Public Domain eBooks
  - Recent Advances In Aids And Kaposi Sarcoma eBook Subscription Services
  - Recent Advances In Aids And Kaposi Sarcoma Budget-Friendly Options
6. Navigating Recent Advances In Aids And Kaposi Sarcoma eBook Formats
  - ePub, PDF, MOBI, and More
  - Recent Advances In Aids And Kaposi Sarcoma Compatibility with Devices
  - Recent Advances In Aids And Kaposi Sarcoma Enhanced eBook Features
7. Enhancing Your Reading Experience
  - Adjustable Fonts and Text Sizes of Recent Advances In Aids And Kaposi Sarcoma
  - Highlighting and Note-Taking Recent Advances In Aids And Kaposi Sarcoma
  - Interactive Elements Recent Advances In Aids And Kaposi Sarcoma
8. Staying Engaged with Recent Advances In Aids And Kaposi Sarcoma
  - Joining Online Reading Communities
  - Participating in Virtual Book Clubs
  - Following Authors and Publishers Recent Advances In Aids And Kaposi Sarcoma
9. Balancing eBooks and Physical Books Recent Advances In Aids And Kaposi Sarcoma
  - Benefits of a Digital Library
  - Creating a Diverse Reading Collection Recent Advances In Aids And Kaposi Sarcoma
10. Overcoming Reading Challenges
  - Dealing with Digital Eye Strain
  - Minimizing Distractions
  - Managing Screen Time
11. Cultivating a Reading Routine Recent Advances In Aids And Kaposi Sarcoma
  - Setting Reading Goals Recent Advances In Aids And Kaposi Sarcoma
  - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Recent Advances In Aids And Kaposi Sarcoma
  - Fact-Checking eBook Content of Recent Advances In Aids And Kaposi Sarcoma
  - Distinguishing Credible Sources
13. Promoting Lifelong Learning



- Utilizing eBooks for Skill Development
- Exploring Educational eBooks

#### 14. Embracing eBook Trends

- Integration of Multimedia Elements
- Interactive and Gamified eBooks

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