Ranibizumab (LUCENTIS) as an Anti-Vascular Growth Factor (Anti-VEGF) in OPHTHALMOLOGY

ESSAY

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INTRODUCTION

Recently the antivascular endothelial growth factor (anti-VEGF) agents, also called antiangiogenic drugs such as pegaptanib sodium (Macugen), bevacizumab (Avastine) and ranibizumab (Lucentis) are the focus of numerous clinical studies attempting to validate their efficacy in mono-or combination therapy protocol in ophthalmology in different eye diseases.

Angiogenesis is a vital part of many physiologic processes during growth and development such as (embryonic development, female menstrual cycle, and wound healing).

Vascular endothelial growth factor (VEGF) is thought to be the most important proangiogenic factor in the body. In addition to stimulating neovascularisation it serves as survival factor for existing vessels.

However angiogenesis with negative effects is found in many diseases such as malignancy, endometriosis, diabetic retinopathy and choroidal neovascularisation. Angiogenesis is maintained in balance by a variety of inducers and inhibitors.[1]

In ophthalmology vascular endothelium growth factor (VEGF-A) has been shown to cause neovascularization and leakage in models of **ocular** angiogenesis and is thought to contribute to the progression of the macular neo-vascularization in AMD.[2] There is also evidence for VEGF overproduction in diabetic retinopathy which has provided a rational therapeutic target to treat Diabetic Macular Edema with anti VEGF.[3]

Blockade of VEGF (vascular endothelium growth factor) mediated angiogenesis has been well established in recent

years as a therapeutic strategy in oncology, and this approach is now available for the treatment of CNV in patients with neovascular AMD and in diabetic macular edema. These agents were originally introduced for the treatment of cancer through the previous mechanism (reduction in endothelial cell proliferation, in vascular leakage and in new blood vessel formation); subsequently cause reduction in the size of the tumor.

The binding of an Anti VEGF to VEGF-A prevents the interaction of VEGF-A with its receptors on the surface of endothelial cells, reducing the endothelial cell proliferation, the vascular leakage, and the new blood vessel formation.[3]

*R*anibizumab (Lucentis) is one of the anti- VEGF drugs widely used nowadays as an intravitreal injection in treatment of AMD and other diseases. It is a derivative of Bevacizumab (Avastin) which is also anti VEGF. Both drugs are derived from the same monoclonal antibody.

Ranibizumab (Lucentis) is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment designed for intraocular administration. The drug is designed to inhibit macular angiogenesis, the growth of new blood vessels in the eye, which can rupture and cause visual loss.

Ranibizumab (Lucentis) has a molecular weight of approximately 48 kilo Daltons and is produced by an *E. coli* expression system in a nutrient medium containing the antibiotic tetracycline. Tetracycline is not detectable in the final product.[3]

In June 2006, the U.S. Food and Drug Administration (FDA) approved Ranibizumab (Lucentis) for the treatment of neovascular wet AMD. The drug received approval in the European Union as the first drug to improve vision in patients with wet AMD in January 2007.

Aim of the work

The aim of this work is to emphasis on Ranibizumab (Lucentis) as a new drug used in ophthalmology as an anti-VEGF. Drug prescription, Clinical Pharmacology, Indications, Doses, Preparation, Administration, Injection procedure, clinical trials, Precautions, Side effects, Ocular and non ocular drug interaction, Over dosage, Contra-indications of the drug all will be discussed.

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استعمال عقار رانيبيزوماب (لوسينتاس) كعقار مضاد لعامل نمو الخلايا المبطنة للاوعية الدموية في طب و جراحة العين

رسالة مقدمه من

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المقدمة

إنتشر حاليا استعمال مجموعة من العقارات تعرف بمضادات عامل نمو الخلايا المبطنة للاوعية الدموية. وتجرى حاليا مجموعة من الأبحاث لمعرفة مدى فعاليتها فى علاج بعض أمراض العيون سواء كانت علاج منفرد اوكعلاج مساعد.

عامل نمو الخلايا المبطنة للاوعية الدموية هو عامل حيوى وهام جدا فى جسم الانسان حيث أنه مسئول عن نمو الأوعيه الدمويه فى الجسم و المحافظه على أداء وظيفتها فى مراحل النمو المختلفه.

يقوم الجسم بالتحكم في نشاط هذا العامل و لكن الزيادة فى نشاط هذا العامل قد يؤدى الى أمراض مثل الأورام أوإزدياد فى تكوين أوعية دموية مرضية تتسبب فى أنزفه وإرتشاحات فى بعض الأنسجة مما يؤثر على وظيفتها.

قد أثبتت الدراسات ان ازدياد هذا العامل فى العين فى الأشخاص الذين يعانون من شيخوخه سنية فى مركز الإبصار هو المتسبب فى تكون الأوعيه الدمويه المرضيه المسئولة عن الأنزفة و الإرتشاحات التى تحدث فى المقولة لهؤلاء المرضى و تتسبب فى ضعف شديد فى الإبصار لديه وكذلك توجد الدلالات على ان ازدياد هذا العامل فى حالات إعتلال الشبكيه السكرى هو المسئول عن الإرتشاحات التى تحدث فى المقولة ايضا. و تؤثر على قوة الإبصار

العقاقيرالتى تعمل كمضادات لعامل نمو الاوعية الدموية أثبتت فاعليتها فى علاج الأورام فى السنين السابقة وحديثا بدأ إستعمالها فى أمراض العيون. .

رانيبيزوماب(لوسينتاس) هو أحد هذه العقاقيرالمعترف بها عالميا منذعام 2006 و التي تستعمل حديثا فى الحقن داخل العين لعلاج الاعتلال الشيخوخى للمقولة وبعض الأمراض الأخرى.

وبالرغم من ان العقار اعطى نتائج مرضية مع بعض المرضى الا انه لابد من معرفة المذيد عنه .

الهدف من هذا العمل

هو عرض لكل ما يتعلق بهذا العقارواستعماله فى طب و جراحة العين.

سيتم وصف العقار. طريقه عمله. الجرعه اللازمة مع عرض دواعى و موانع الاستعمال . طريقة تحضير و حقن العقار. الاحتياطات اللازمه فى استعماله. الاعراض الجانيبية .المضاعفات المتوقعة مع عرض نتائج الدراسات السابقه .

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Yasmine Maher

List of Abbreviations

AEs	Adverse Events
AMD	Age Related Macular Degeneration
ANCHOR	Predominantly Classic Choroidal Neovascularization

List of Abbreviations	
APTC	Anti platelet Trialists Collaboration
ANCHOR	Anti-VEGF Antibody for the treatment of predominantly Classic Choroidal Neovascularization in AMD
BCVA	Best Corrected Visual Acuity
BRVO	Branch Retinal Vein Occlusion
BRAVO	Branch Retinal Artery and Vein Occlusion
CNV	Choroidal Neo-Vascularization
CRT	Central Retinal Thickness
CSC	Central Serous Chorioretinopathy
DDME	Diffuse Diabetic Macular Edema
DLL4	Delta Like Ligand 4
DME	Diabetic Macular Edema
ETDRS	Early Treatment Diabetic Retinopathy Study
GS 101	Gene Signal Anti sense oligonucleotide
ICGA	Indo Cyanin Green Angiography
INV	Iris Neovessels
IVB	Intravitreal Bivacizumab
IVP	Intravitreal Pegaptanib
IVR	Intravitreal Ranibizumab
FA	Fluorescein Angiography
FRT	Foveal Retinal Thickness
HIF	Hypoxia Inducible Factor
HUVEC	Human Umbilical Vascular Endothelial Cell

MARINA	Minimally Classic Occult Trial of Ranibizumab in Treatment of Neovascular AMD
ME	Macular Edema
MMP	Matrix Metallo Proteinase
MTD	Maximum Tolerated Dose
Mcnv	Myopic Choroidal Neovascularization
NEIVFQ	National Eye Institute Visual Function Questionaire
NV 1FGF	Non Viral Growth Factor
NV	New vascularization
NVG	Neo-Vascular Glaucoma
OCT	Optical Coherent Tomography
QOL	Quality Of Life
PDGF	platelet-Derived Growth Factor
PDR	Proliferative Diabetic Retinopathy
PDT	Photodynamic Therapy
PLGF	Placenta Growth Factor
PRP	Pan Retinal Photocoagulation
RP	Retinitis Pigmentosa
RPE	Retinal Pigment Epithelium
RT	Retinal Thickness
US	Ultra Sound
TKI	Tyrosine Kinase Inhibitor
SAEs	Serious Adverse Events
VPF	Vascular Permeability Factor
VEGF	Vascular Endothelial Growth Factor
VEGFR	Vascular Endothelial Growth Factor Receptor
VISION	VEGF Inhibition Study In Ocular Neovascularization