Synthesis of flutamide-conjugates.

Related Articles

Synthesis of flutamide-conjugates.
Bioorg Med Chem Lett. 2020 Aug 28;127507
Authors: Medina-Rojas JC, Castillo-Rodríguez IO, Martínez-Klimova E, Ramírez-Ápan T, Hernández-Ortega S, Martínez-García M

Abstract
In this paper, we designed and extended modification basing on the flutamide structure. A series of flutamide-conjugates were obtained with methyl bromoacetate and ethylenediamine. Through the synthesis of two conjugates with 3,5-bis(dodecyloxy)benzoate derivatives, these flutamide conjugates were tested for anticancer activity. Among the compounds tested, the flutamide-conjugates showed good inhibition activity against cancer cell lines U-251, PC-3 and K-562. The conjugates showed a better inhibitory effect than free flutamide and did not show activity against normal COS-7 monkey kidney fibroblast cells. It was also observed that the flutamide conjugates had an inhibitory effect against human colorectal adenocarcinoma HCT-15.

PMID: 32866675 [PubMed — as supplied by publisher]

Double Mandibular Osteotomy for Access to High-Carotid Pathology.

Related Articles

Double Mandibular Osteotomy for Access to High-Carotid Pathology.
Ann Vasc Surg. 2020 Aug 28;:

Abstract
BACKGROUND: Anecdotal experience demonstrates the existence of patients with superiorly located carotid stenosis, neoplasms, or aneurysms where the mandible obstructs effective surgical access using standard techniques. As carotid pathology extends anatomically beyond the limits of standard operative technique, additional exposure becomes paramount to safely and effectively address the lesion. Double mandibular osteotomy (DMO) is one of several techniques to obtain additional exposure to high-carotid pathology however there is no large series to address the outcomes of patients undergoing this procedure.

PATIENTS AND METHODS: A retrospective case series was performed of all patients undergoing surgery for carotid pathology from 2011 — 2019 that could not be approached with standard cervical incision. The primary predictor variable was high anatomic carotid pathology necessitating DMO. The primary outcome variable was early and late complications sustained by patients.

RESULTS: Fifteen patients met study criteria and underwent 16 DMOs to access high-carotid pathology including carotid stenosis (n=8 patients), carotid aneurysm (n=2 patients), and carotid body tumor (n=8 patients). Two patients had dual ipsilateral pathology with one patient having both carotid artery stenosis and aneurysm, and the other patient diagnosed with carotid artery stenosis and carotid body tumor. One patient had bilateral carotid artery stenosis, each requiring high anatomic exposure for treatment. Early complications occurred in eight patients. Five patients experienced significant dysphagia requiring enteral feeding and two patients developed malocclusion directly related to the double mandibular osteotomy. One patient experienced contralateral cortical watershed infarcts. Late complications included one patient developing osteomyelitis of the mandible and this patient also developed distal mandibular segment screw exposure. The comparison of the outcome groups for categorical predictor variables using Fisher’s Exact Test detected no statistically significant differences for gender, hypertension, hyperlipidemia, type 2 diabetes, COPD, tobacco use, chronic kidney disease, or cerebrovascular disease. For the continuous variable comparisons, independent-samples t-tests detected no difference between the complication groups for age, operative time, or years of follow-up. No significant differences were found between the groups for body mass index, or intraoperative blood loss.

CONCLUSION: The double mandibular osteotomy provides excellent exposure and surgical access to the distal internal carotid artery for repair of vascular pathology with acceptable outcomes and long-term complications compared to previously reported techniques. Due to the early complications realized with the DMO, we recommend the procedure for symptomatic patients with a high risk of failing medical therapy alone and not appropriate for endovascular treatment as well as those patients with tumors requiring surgical intervention.

PMID: 32866578 [PubMed — as supplied by publisher]
Germline HSD3B1 Genetics and Prostate Cancer Outcomes.

Related Articles

Germline HSD3B1 Genetics and Prostate Cancer Outcomes.

Urology. 2020 Aug 28.;
Authors: Thomas L, Sharifi N

Abstract
Dihydrotestosterone synthesis in prostate cancer from adrenal
DHEA/DHEA-sulfate requires enzymatic conversion in tumor
tissues. 3β-hydroxysteroid dehydrogenase-1 (3β-HSD1) is an
absolutely necessary enzyme for such dihydrotestosterone
synthesis and is encoded by the gene HSD3B1 which comes in two
functional inherited forms described in 2013. The
adrenal-permissive HSD3B1(1245C) allele allows for rapid
dihydrotestosterone synthesis. The adrenal-restrictive
HSD3B1(1245A) allele limits androgen synthesis. Studies from
multiple cohorts show that adrenal-permissive allele inheritance
confers worse outcomes and shorter survival after castration in
low-volume prostate cancer and poor outcomes after abiraterone
or enzalutamide treatment for castration-resistant prostate cancer.
Here, we review the clinical data and implications.
PMID: 32866512 [PubMed — as supplied by publisher]

Author Reply: 3D Printing, Augmented Reality, and Virtual Reality for the Assessment and Management of Kidney and Prostate Cancer: A Systematic Review.

Related Articles

Author Reply: 3D Printing, Augmented Reality, and Virtual Reality for the Assessment and Management of Kidney and Prostate Cancer: A Systematic Review.

Urology. 2020 Aug 28.;
Authors: Wake N, Bjurlin MA
PMID: 32866508 [PubMed — as supplied by publisher]

Male sex, severe obesity, older age, and chronic kidney disease are associated with COVID-19 severity and mortality in New York City.

Related Articles

Male sex, severe obesity, older age, and chronic kidney disease are associated with COVID-19 severity and mortality in New York City.

Chest. 2020 Aug 28.;
Authors: Rapp J, Lieberman-Cribbin W, Tuminello S, Taioli E
PMID: 32866462 [PubMed — as supplied by publisher]

Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial.

Related Articles

Carfilzomib or bortezomib in combination with lenalidomide and dexamethasone for patients with newly diagnosed multiple myeloma without intention for immediate autologous stem-cell transplantation (ENDURANCE): a multicentre, open-label, phase 3, randomised, controlled trial.

Lancet Oncol. 2020 Aug 28.;

Abstract
BACKGROUND: Bortezomib, lenalidomide, and dexamethasone (VRd) is a standard therapy for newly diagnosed multiple
myeloma. Carfilzomib, a next-generation proteasome inhibitor, in combination with lenalidomide and dexamethasone (KRd), has shown promising efficacy in phase 2 trials and might improve outcomes compared with VRd. We aimed to assess whether the KRd regimen is superior to the VRd regimen in the treatment of newly diagnosed multiple myeloma in patients who were not being considered for immediate autologous stem-cell transplantation (ASCT).

METHODS: In this multicentre, open-label, phase 3, randomised controlled trial (the ENDURANCE trial; E1A11), we recruited patients aged 18 years or older with newly diagnosed multiple myeloma who were ineligible for, or did not intend to have, immediate ASCT. Participants were recruited from 272 community oncology practices or academic medical centres in the USA. Key inclusion criteria were the absence of high-risk multiple myeloma and an Eastern Cooperative Oncology Group performance status of 0–2. Enrolled patients were randomly assigned (1:1) centrally by use of permuted blocks to receive induction therapy with either the VRd regimen or the KRd regimen for 36 weeks. Patients who completed induction therapy were then randomly assigned (1:1) a second time to either indefinite maintenance or 2 years of maintenance with lenalidomide. Randomisation was stratified by intent for ASCT at disease progression for the first randomisation and by the induction therapy received for the second randomisation. Allocation was not masked to investigators or patients. For 12 cycles of 3 weeks, patients in the VRd group received 1.3 mg/m² of bortezomib subcutaneously or intravenously on days 1, 4, 8, and 11 of cycles 1–8, and day 1 and day 8 of cycles nine to twelve, 25 mg of oral lenalidomide on days 1–14, and 20 mg of oral dexamethasone on days 1, 2, 4, 5, 8, 9, 11, and 12. For nine cycles of 4 weeks, patients in the KRd group received 36 mg/m² of intravenous carfilzomib on days 1, 2, 8, 9, 15, and 16, 25 mg of oral lenalidomide on days 1–21, and 40 mg of oral dexamethasone on days 1, 8, 15, and 22. The coprimary endpoints were progression-free survival in the induction phase, and overall survival in the maintenance phase. The primary analysis was done in the intention-to-treat population and safety was assessed in patients who received at least one dose of their assigned treatment. The trial is registered with ClinicalTrials.gov, NCT01863550. Study recruitment is complete, and follow-up of the maintenance phase is ongoing.

FINDINGS: Between Dec 6, 2013, and Feb 6, 2019, 1087 patients were enrolled and randomly assigned to either the VRd regimen (n=542) or the KRd regimen (n=545). At a median follow-up of 9 months (IQR 5–23), at a second planned interim analysis, the median progression-free survival was 34·6 months (95% CI 28·8–37·8) in the KRd group and 34·4 months (30·1–not estimable) in the VRd group (hazard ratio [HR] 1·04, 95% CI 0·83–1·31; p=0·74). Median overall survival has not been reached in either group. The most common grade 3–4 treatment-related non-haematological adverse events included fatigue (34 [6%] of 527 patients in the VRd group vs 29 [6%] of 526 in the KRd group), hyperglycaemia (23 [4%] vs 34 [6%]), diarrhoea (23 [5%] vs 16 [3%]), peripheral neuropathy (44 [8%] vs four [