The Emerging Role of Anticancer-Drugs-Bexarotene in a Clinical Trial of Alzheimer's Dementia

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Abstract

Background: Cancer is a disease which affects the elderly, just like Alzheimer's disease (AD) which is also a common disease affecting older people. Most of the symptoms are related with both these diseases, therefore there may be therapeutic link between anticancer drugs and AD.

Objective: To synthesize the studies aimed at therapeutic links between Alzheimer's disease and anticancer drugs (Bexarotene).

Design: To identify potential new treatment possibilities we applied the systematic searches of key electronic databases. The inclusion criteria were;

a. Studies aimed at improving cancer and anticancer therapies with human model.

b. Peer-reviewed and written in English without any searching limitation on the basis of published date.

c. Studies of drugs related to cancer treatment that was relevant to AD.

d. We did not include the clinical news, case report and animal trial studies.

Results: After filtering titles, abstract, references published in English into one study that has been condensed into one volume of literature. There is very hard to find studies aimed at therapeutic links between Alzheimer's disease and Anti-cancer drugs in human model. However, sufficient studies are conducted with animal model (mice) and indicating the positive benefits to the AD patients. Bexarotene is useful for the reduction of cholesterol, loss of function associated with APOE ε4, peripheral thyroid hormone metabolism and athyreotic and amyloid beta that is a key cofactor of Alzheimer's disease. Also, Bexarotene has been shown to restore cognitive functions.

Conclusion: This review discusses the emerging role of anticancer-drugs-Bexarotene in a clinical trial of Alzheimer's dementia with the support of animal model successful results and their effectiveness and will be a significant drug in the coming decades.

Keywords: Anti-cancer therapy; Alzheimer's disease (AD); Dementia

Objective: To synthesize the studies aimed at therapeutic links between Alzheimer's disease and anticancer drugs.

Introduction

Cancer and Alzheimer's disease are associated with aging [1] and are becoming more common. Cancer is one of the most dreaded non-communicable disease and the important contributor to the global burden of diseases as well as one of the leading causes of death worldwide. It is among the leading cause of death worldwide, with approximately 14 million new cases and 8.2 million cancer-related deaths in 2012 [2]. Cancer brings tremendous social distress, physical & psychological suffering, hardship to patients and their relatives. The relationship between dementia and cancer is complex [3] to define due to the overlapping characteristics. It has an inverse relationship and most cases are under diagnosed. Individuals with cancer and dementia demonstrate unique challenges due to poor communication difficulties, mild cognitive impairment and 'chemo brain', progressive neurodegeneration, and cognitive function etc. Therefore, quality assessment is necessary, including cognitive function for both dementia and cancer patients [4].

Likewise, AD has no gold standard treatment (with an overall failure rate 99.6%) [5] like cancer does. This means that there are several drugs presently in trials and have shown promise as possible modifiers of disease progression [6]. However, anticancer chemotherapy often induces peripheral neuropathy and as a consequence cognitive decline and finally quality of life is impaired. Commonly anti-epileptics or anti-depressants are recommended, but their efficacy is not satisfactory [7]. Going forward, whether anti-cancer therapy can reverse AD remains to be scientifically proven. No cure exists for AD, but scientists are showing new alternative ways in animal studies those show that cancer drugs are able to reduce neurodegeneration, raising the possibility of repurposing those agents for use in AD. It is found that drugs which reach the brain, took the role of tau stabilized microtubules in the animals' brains. This led the scientists to conclude that the molecules from these classes could be appropriate drug candidates for treating AD and related disorders [8].

In 2013 Kemsley showed Apo lipoprotein ε4 (APOE ε4) and APOEε3, increased memory power with the use of Bexarotene. Bexarotene is a compound chemically related to vitamin A that activates Retinoic X Receptors (RXR) found everywhere in the body and rapidly cleared amyloid plaques from the brains of Alzheimer's model mice [9]. The next study's aim was to assess (within 20 population) the safety and effects on the brain for the drug Bexarotene as a possible treatment for AD. People were given either 300 mg of the anti-cancer drug Bexarotene or a placebo for 1 month and underwent brain scans to determine the drug's effectiveness on the brain. Bexarotene acts to reduce harmful beta-amyloid protein deposits in the brain in experimental models of AD by inhibiting retinoid X receptors, nuclear receptors that have been linked to numerous metabolic pathways relevant to AD and beta-amyloid production and removal [10].

A recent study found that an anti-cancer drug was effective in reversing the memory deficits in an AD mouse model. Bexarotene, which commonly used to fight lymphoma, significantly improved the cognitive deficits in mice expressing gene mutations linked to human AD. They believe that these findings make a solid case for continued exploration of Bexarotene as a therapeutic treatment for AD. Mice treated with Bexarotene-a retinoid approved to treat skin problems caused by T-cell lymphoma- recovered from AD. Mice rapidly gained in intelligence while plaque in their brains, causing the disease began within hours to disappear, boosting levels of Apo lipoprotein E that helps clear build-up of amyloid plaque in the brain [11].

Likewise, next study [12] claimed that skin cancer drugs treat late-stage dementia in Mice. Scientists declared that a mouse is the best animal model to show the hints of improvement in AD. The genetically engineered mouse carries a human gene that increases the risk of AD by 15 times. Researchers explained that humans generally carry a gene of Apo lipoprotein E in cells,

which helps to clear amyloid-beta in the brain by binding it and destroying it. One study revealed a 40 percent decrease in levels of soluble amyloid-beta and an increase in the binding of Apo lipoprotein in amyloid-beta in mice at the later stages of AD.

Kopman (2013), suggested that a Cancer drug is not a miracle cure for AD [13], but there is still some hope between Bexarotene and AD. They tested Bexarotene on mice to assess the effects on the brain, especially on AD plaques. The result showed that beta amyloid plaques in the brain were reduced. While mice with Alzheimer's-like brain damage were given Bexarotene orally, they were able to reverse cognitive and social deficits and clear more than half of the beta-amyloid peptides from the brain within 72 hours [14]. Bexarotene, in the current practice showed a great evidence to bring the greater rate of clearance of ß-amyloid plaques over the time significantly [15] and result was based on murine model of AD.

There is another study Bexarotene resulted a significant reduction in the level of the neurotoxic amyloid- beta in the late-stages of AD for mice [16]. In adult patients, cancer brain toxicity remains a major cause of morbidity. Additionally, drugs used in non-brain tumours are now recognized to impair the normal functioning of brain [17]. A review on efficacy and safety of pharmacotherapy in cancer-related psychiatric disorders across the trajectory of cancer care concluded that 25–30% of patients with cancer in an advanced phase of illness met the criteria for a psychiatric disorder like; depression, anxiety, stress-related syndromes, adjustment disorders, sleep disorders and delirium. A review study, on psycho-oncology research has shown the efficacy of psychotropic drugs as adjuvant treatment of cancer-related symptoms, e.g.; pruritus, nausea and vomiting, pain, hot flashes, fatigue, and cognitive impairment, etc [18].

Another study [19] showed the therapeutic positive link between AD and cancer patients, who were survivors of breast cancer and using cancer drugs-s had a lower risk of AD after using anti-cancer drugs. Likewise, a landmark paper was published in Science showed Bexaro¬tene, to treat cutaneous T-cell lymphomas, created potential new hope for the treatment of AD [20]. Additionally, next two studies [21, 22] agreed that cancer survivors had a lower risk of AD than those without cancer, and patients with AD had also a lower risk of cancer.

We see the association between AD and cancer on the clinical praxis of symptoms. Likewise, one study showed a result of breast cancer of woman who received adjuvant chemotherapy had a higher likelihood of dementia after long-term follow-up [23]. These findings shed light on a cure and warrants analysis of the consequences of this hypothesis, not only from the viewpoint of drug discovery for new treatments, but above all, the awareness that any AD chemotherapy will require drug administration over longer periods of time before any cognitive effects are observed. Because such drugs will probably act as neuro protective agents, slowing the progression of AD rather than curing it, they should be prescribed as soon as the first AD symptoms are detected.

After conducting a preliminary survey of anticancer therapy that have potential value for AD, new drugs that affect specific signal transduction pathways known to be activated by anticancer drugs could be identified, with the unfolding protein response pathway being one of the most relevant biological targets for new AD chemotherapeutic agents.

Most AD criteria are based on dysfunction of cognitive ability as well as a significant impact on social functioning and activities of daily living. Conducted human model research with cancer is showing significant proof of the minimising effects of cognitive impairment. The majority of the above-mentioned mice studies do not necessarily translate to human models. Further, animal model research requires for more testing, but the human benefits of Bexarotene and AD are still years away. Some human studies for those with cancer and treated with chemotherapy have shown positive signs in cognitive improvement and some of those animal (mouse) model studies conducted in mice also show positive signs of cognitive improvement [24]. Much research remains to be done, but even if, Bexarotene (chemotherapy) is found to be effective at reducing cognitive impairment as a treatment for AD in humans, it has opened the door to find a new treatment approach to the pathology of this disease and, in fact, may one day represent a new class of AD therapies. Dozens of questions have been raised, however these must be addressed in a coming study- how does Bexarotene (chemotherapy) improve cognition and other symptoms that appear with AD patients?

The present review is a systematic review of anti-cancer drug and AD aimed at improving the AD related symptoms with the patients. Before this review, a review conducted to describe and discuss the literature addressing the effects of Bexarotene in AD model of mice and showed its potential clinical implications [25]. But we only focus on human model studies in this review. We took a broader review and do not restrict it to any studies with cancer and AD related symptoms. All the aforementioned original studies focus on animal model to measure the effectiveness, often find that the evidence is somewhere mixed or somewhere positive, and provide clues for future AD agent. Furthermore, most cancer patients who were consuming chemotherapy was seen significant to increase the memory issues. That is why, the review worked to find an emerging model of research synthesis "realist review" [26,27], which is designed to work with complex relationships between Alzheimer's and cancer drugs, and which is aimed at penetrating what drugs, to whom, in what circumstances, in what respects and how.

Additionally, many pharmaceutical companies have downsized the option for new Alzheimer's treatments after the false step of several eminence exorbitant trials. It was essential to do review study, since last decades there has been the failure rate (99.6%) [28] in AD treatment. This, however, might have a proposed a trend of exploring drugs that have already been approved by the US Food and Drug Administration for other hints, but that can be interacted with physiopathology through mechanisms unrelated to their original therapeutic indication. Since Bexarotene (chemotherapy) have already gone through clinical practice trials or pipeline, which can breakthrough in the AD patients [25].

Methods

Search Strategy

The aim of this systematic review was to retrieve the studies that are related to cancer drug with dementia and AD and to ascertain whether any improvement exists in AD patients' results. Relevant articles were retrieved following searches of databases: PubMed, PsychInfo, Medline, Scopus, Google search engine, Cochrane library. Titles and abstracts were examined, and then full texts were retrieved for potentially relevant studies and these were assessed. As this is the first systematic review undertaken to evaluate the existing evidence on the therapeutic link between cancer drugs and AD, the search strategy used a broad-brush approach using overarching terms/keywords. The use of overarching terms/ keywords ensured that all potentially relevant articles were included in the initial screening.

To identify potential new treatments we applied the following: Anti-cancer drugs and dementia, anti-cancer and AD, Anti-cancer and cognitive, chemotherapeutic agents and Alzheimer, Breast cancer and Cognitive impairment, Cancer and language impairment, Cancer and language praxis, Bexarotene and gastrointestinal complication, Cancer drugs and language impairment, Bexarotene and pain, Cancer drugs and cognitive, doxorubicin and Alzheimer, Cancer drugs and dementia, Cancer drugs and AD, Cancer drugs and Apo lipoprotein, Liver cancer and lipoprotein, Chemotherapy and dementia, Chemotherapy and Alzheimer disease, Bexarotene and Alzheimer disease, Cancer therapy and Alzheimer Cochrane, Anticancer drugs and dementia, doxorubicin and Alzheimer, Anticancer drugs and cognitive impairment, Chemotherapy drugs and cognitive impairment, Cancer therapy and Alzheimer, Cancer drugs and dementia, cyclophosphamide and Alzheimer, Anti-cancer and cognitive impairment, Chemotherapy and dementia.
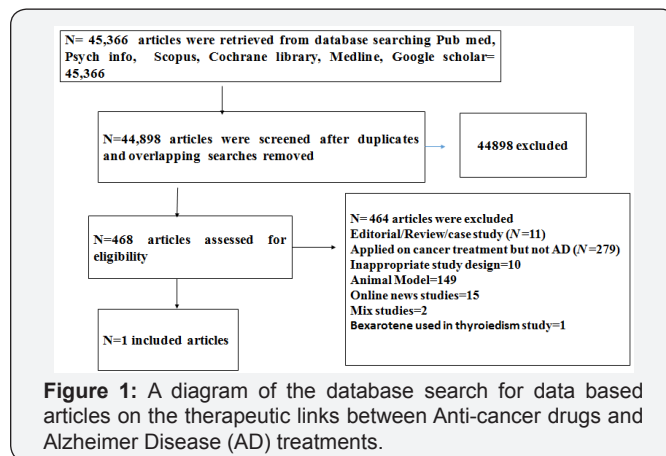

Figure 1: A diagram of the database search for data based articles on the therapeutic links between Anti-cancer drugs and Alzheimer Disease (AD) treatments.

In all databases, the search was restricted to articles where the keywords were the major focus of the article. A similar search strategy was used in the remaining databases. In addition, we reviewed the reference lists of previous reviews to identify potentially eligible studies. Publication studies were included to any active cancer treatment e.g.; chemotherapy, breast cancer, cognitive deficit, brain cancer, cervical cancer, hormonal therapy and therapy with molecular-targeted agents and any combinations of cancer which were related with AD symptoms and treated with cancer drugs. We did not include those studies showing significant results to the AD patients on the basis of (mice) animal model, online news, case studies, uncompleted experimental studies and their expectation results (Figure 1). Table 1 is describing some related studies (case studies, uncompleted experimental studies and their expectation results) with Bexarotene because that will be helpful to understand to the reader how it is very close for new treatment of AD.

Table 1: Useful study and expected results regarding on AD related symptoms. But these studies are not conducted fully with AD patients- it is tested with some kinds of AD related issues. These are case report, a clinical news etc for those we did not included in your study because we can give a not result of study and claim for proof.

No	Study	Aim	Participant	Study design and methods	Results	Conclusion
1	Babak Tousi, (2014) United States.	To find the Bexarotene for the treatment of cognitive for the treatment of cognitive decline in an individual with Alzheimer's dementia.	Female 79, (breast cancer and hypertension) with history of memory loss for 10 years, diagnosed with Alzheimer's dementia 7 years ago.	Case report, stopped Aricept and Namenda then was started on Bexarotene 150 mg daily and continued for 3 months. blood tests, liver function test, lipid panel, Blood cell count and thyroid function tests were done at baseline and repeated at week 2, week 6, week 8 and after 3 month treatment and	No noticeable change in labs except the gradual increase in cholesterol level. Omega-3-acid was stared as preventive measure for hyper triglyceridemia at week 2, Atorvastatin 10 mg for week 6 to treat hypercholestrolemia. result shoed more interactive on week 6 visit, MOCA and ADAS-Cog score did not show any significant change during this period. gradually developed more behavioral symptoms like; sun downing.	Bexarotene was well tolerated, but did not improve cognition of our patient in moderately severe stage of Alzheimer's dementia. The patient only Developed hypercholesterolemia which responded well to statin therapy. There was worsening of behavioral symptoms which continued after discontinuation of drug, which may be related to the progression of dementia.
2	Johannes WA Smit et al. (2007)	To evaluate the effects of bexarotene on peripheral thyroid hormone	Ten athyreotic patients. with pulmonary metastases of differentiated thyroid carcinoma received 6-wk redifferentiation treatment with 300 mg bexarotene	an open an open prospective 6-week intervention with ten athyreotic patients with pulmonary metastases of differentiated thyroid carcinoma received 6-wk redifferentiation treatment with 300 mg bexarotene/d. L-T4 doses were kept stable. Before and in the sixth week of therapy, serum levels of total T4, free T4 (FT4), T3, reverse T3 (rT3), and TSH were measured.	Bexarotene induced Bexarotene induced profound decreases in total T4 (56% of baseline), FT4 (47%), T3 (69%), rT3 (51%), and T4S (70%) in all patients, Whereas TSH levels were not affected. The T3/rT3 ratio increased by 43%, and the T4S/FT4 ratio increased by 48%. Serum TSH levels before	In the present study In the present study, we demonstrate that increased peripheral degradation of thyroid hormones by a nondeiodinase-mediated pathway contributes to bexarotene induced-hypothyroidism.

3	Craig T Curtis (2014)	Objective of this proof of Objective of this proof of mechanism pilot clinical trial is to determine if the RXR agonist bexarotene acts in humans to alter the CSF levels of apoE and alter the clearance of Amyloid-Beta	• Experimental with 12 populations age 21-50 years, APOE3/3 genotype	A Randomized Controlled Study, A Randomized Controlled Study, AD patients, Bexatorend drugs Experimental: Bexarotene The subjects will be administered three (3) capsules of Targretin™ (75 mg/capsule) on a twice daily basis (450 mg/day) for five days. Placebo Comparator: Placebo The subjects will be administered three (3) capsules of Avicel PH on a twice daily basis (450 mg/day) for five days.	The expected result -Will be effective drug	The excepted conclusion-Will be effective drug.
4	Jeffrey L Cummings, and Kate Zhong, (2013) Cleveland Clinic Lou Ruvo Cente, Braitian.	To determine the safety and effect on the To determine the safety and effect on the brain of the drug bexarotene as a possible treatment for Alzheimer's disease.	20 mild to moderate AD	Bexarotene for Alzheimer Disease: Bexarotene for Alzheimer Disease: Innovative Clinical Trial Could Open the Door to Disease-Modifying. In 2nd trial 300mg for and 1 month (Double Blind Placebo Controlled Randomized Study) to Evaluate the Efficacy and Safety of Bexarotene.	Bexarotene can be applied in new ways for AD Patients.	Bexarotene is safety and effect on the brain of the drug bexarotene as a possible treatment for Alzheimer's disease.

Results

Included Studies and Characteristics

The broad all above mentioned searches yielded 45,366 citations, those were reduced after filtering titles, abstract, references published in English. Once the abstracts were reviewed for relevance, duplicate publications removed. This systematic review has established that there is very little literature (N=1) [29] published in this area up to now. The inclusion criteria in this study was identified a dearth of treatment based on cancer and symptoms of AD. This systematic review identified just (N=1) one study and illustrated in the (Table 2). The study was measured the cancer treatment patients and showed a positive result in reducing the common symptoms between cancer and AD. That study was from France and a summary of the study abstract is displayed in the table text. This study adds that the Bexarotene helped to improvement in cognitive impairment, reduced cholesterol levels, pulmonary metastases, thyroid functions and hypothyroidism in the patients who were consuming the Beaxarotene. Maximum studies were conducted with animal studies (mice model) and some were published as current news on online news but we did not include in our study however we have shown these studies in table 2 that might be fruitful as a witness to show the possibility of b Beaxarotene in the coming days (Table 2).

Table 2: Some useful studies Characteristics and their expected results.

Study	Aim	Participant	Title	Study design and methods	Results	Conclusion
Jacques Fantini et al. (2014) France	To find combination of Bexarotene combination and Alzheimers'Amyloid Peptides.	Not stated	Bexarotene blocks calcium-permeable ion channels formed by neurotoxic Alzheimer's β-amyloid peptides.	It is The experimental approach. it's combination of molecular, physicochemical, and cellular approaches to elucidate the mechanisms underlying the anti-Alzheimer properties of Bexarotene in neural cells	Bexarotene and cholesterol interact with the same region located in C-terminal domain of Aβ1−42 and share the same binding site on Aβ.	Cholesterol, and amyloid beta a key Cofactor of Alzheimer's disease. Bexarotene has been shown to restore cognitive functions.

Discussion

This is the first systematic review to assess cancer drugs in association with AD. We retrieved many studies representing a huge range of successful cancer treatments mostly focused on hormonal therapy for women with early-stage breast cancer [30,31] impaired cognitive function and hippocampal neurogenesis [32] CNS cancer [33] cognitive impairment, brain structure and risk of dementia [34] cervical cancer, cognitive problem/impairment [35], gastro intestinal in complication, to maintain haemoglobin level, menopausal status [36] and other types of cancers but none specifically with AD. Also, we retrieved a huge range of animal studies- all of which showed future ways for treating humans with AD [37,38]. However, we did not include the animal studies here in this study because our intention was to evaluate cancer therapy for people affected with AD and the possible links between Anti-cancer drugs and AD.

However, questions remain unanswered about the benefits and risk of anti-cancer drugs (Bexarotene's) when used on patients affected with AD. Also, of interest is how much reduction in Aβ synthesis needs to occur to produce a cognitive benefit? What is surprising is that only one study examined Bexarotene (chemotherapy group) therapy is known to affect cancer patients and AD patients. However, doxorubicin and cyclophosphamide- for the treatment of chronic lymphocytic leukemia, bladder, breast, head and neck, thyroid, uterus, liver, lung, lymphomas, mesothelioma, ovary, pancreas, prostate, multiple myeloma, neuroblastoma, sarcomas, stomach, testis -germ cell [39], a chemotherapy Imatinib- reduced Aβ-β-amyloid protein/ neuro protective, paxclitaxel treatments of ovarian carcinoma, breast cancer, lung cancer, kaposis's sarcoma are potential agents in the coming decade. A review study [40] found at least 25-30% of patients with cancer meet also the criteria of a psychiatric condition including depression, anxiety, stress-related syndromes, adjustment disorders, sleep disorders, pain, hot flashes, puritus, nausea and vomiting, fatigue, cognitive impairment and delirium. Psycho-oncology research showed the efficacy of psychotropic drug treatment of cancer-related symptoms. Therefore, we may generalize that the vast majority of the above-mentioned symptoms frequently appear also in AD patients. That means that treatments for those who have cancer and are using psychotropic drugs might also be beneficial for those who are AD patients.

Likewise, Tropisentron [2 mg (IV) intravenous and 5mg oral] -antagonist used as an antiemetic to treat nausea and vomiting following chemotherapy [41] promoted positive improvement in memory compared to conventional AD therapy, like memantine and donepezil. Some exceptions include- anti diabetics drugs-lixisenatide, exenatide; anti-hypertensive- angiotensin enzyme inhibitors and receptors blocker, hydroclorothiazide, Enalpril, amlodipine, isradipine; anti-viral- acyclovir, penciclovir, foscarnet; anti-microbial- rifampin for microbacterium infection [42], hydroxiclroquine, amphotericin B, erythromycin, tertacyline- minocycline [43] Glucose disaccharide-threhalose; anti-oxidant (PD)-pramipexol; anti-psychotic- quetiapine, olanzapine, risperidone and anti-asthamic- zileuton [44].

Another dozen medicines are being used with mice (animal models) and are showing significantly improving results in the treatment of AD related data in different study models [45-47]. Additionally, there are currently many drugs in the preclinical stages of development, and more than 100 have progressed to human testing Pharma Report (2010). Most clinical diagnosis trials of AD agents have not been showing successful results however the cholinesterase inhibitors and memantine showed symptomatic improvement for AD patients. In a few cases, unsuitable trials were applied inadequately when testing the trial agent, while with other trials which were suitably applied there was no proof of efficacy.

French research revealed [29] that cholesterol and Bexarotene compete for the same bind¬ing site in the C-terminal region of Aβ1-42 which is a protein highly correlated with AD.

Bexarotene competed with cholesterol for binding to Aβ and prevented neurotoxic oligomeric formation of Aβ. Likewise, further research showed Bexarotene was able to counteract both Aβ-induced and Aβ-independent increases in cortical net¬work hyper excitability. A current study on "the emerging role of Bexarotene in the treatment of AD: current evidence" found that Bexarotene, a retinoid X receptor agonist, was shown to reverse neurodegeneration, improve cognition, and decrease levels of amyloid-β in transgenic mice expressing familial AD mutations.

A case report of a woman 79 years old with breast cancer and hypertension and history of memory loss for 10 years, diagnosed with AD 7 years ago of application of Bexarotene 150 mg/d for 3 months. Blood tests, liver function test, lipid panel, blood cell count and thyroid function tests at baseline and repeated at week 2, week 6, week 8 and after 3 months of treatment showed no noticeable change in lab testing and cognition except the gradual increase in cholesterol levels and meaningful change of behavioural symptoms-sun downing. So, we can say Bexarotene was well tolerated. Furthermore, Bexarotene therapy is good for coming drug development in AD treatment, due to its high blood–brain barrier perme¬ability and current safety profile. Bexarotene induced profound decreases in total T4 (56% of baseline), FT4 (47%), T3 (69%), rT3 (51%), and T4S (70%) in all patients, whereas TSH levels were not affected. The T3/rT3 ratio increased by 43%, and the T4S/FT4 ratio increased by 48%.

A study has been conducted at the Clevent Clinic, Las Vegas Nevada to determine the safety and effect on the brain of the drug Bexarotene as a possible treatment for AD patients with the min age 50 and max age 90, in both males and females using a double-blind placebo controlled randomized study to evaluate the efficacy and safety of Bexarotene in patients with mild to moderate AD. The expected result of that study will come later the mid-year 2015. In the preliminary phase of study patients will receive 300/mg of the anti-cancer drug Bexarotene or a placebo for 1 month and brain scans- hope is that Bexarotene acts to minimise the harmful Aβ protein in the brain; also retinoid X receptors and nuclear receptors will have been connected to numerous metabolic pathways relevant to AD and Aβ production and removal.

Although there have been many studies on cancer treatments, these have not focused on all forms of active cancer treatment association with AD populations. The strengths of this review include the systematic methodology used to identify all relevant articles from multiple databases and have very few limitations with respect to scientific quality of the studies included. Also, we have not used meta-analysis studies for outcomes. In conclusion, cancer therapy is new approach for the treatment of AD and currently mostly these are in preclinical studies and early phases of clinical trials. With this study, we learn more detail about the chemotherapy and disease progression of AD symptoms and an insight into the potential therapeutic evidences. Despite the fact that the bulk knowledge on regarding this chronological disease,

only a handful recourse is available for its treatment. The presently applied drugs, Acetylcholinesterase and Buturylocholinesterase Inhibitors for the treatment unfortunately target symptoms only and not the cause of the disease. The hope was significant for AD treatments [27] because chemotherapy drugs are successful at treating cutaneous T-cell lymphomas, cognitive impairment and has been shown to have benefits in mouse models of AD. For the human clinical trials it is still extremely premature to expect effective treatment for AD because of recent warnings for Bexarotene.

Conclusion

This conclusion presents the strong witness from animal models. However, the perfect model would be on human model studies for the prescription to the AD patient's because animal model is not sufficient to meet all of the clinical criteria. We found a study that was observed combination of molecular, physicochemical, and cellular approach to examine the mechanisms of underlying the anti-Alzheimer properties of Bexarotene in neural cells and Bexarotene was showed to restore cognitive functions. Obviously, we cannot do refer 100 percent to the AD patient due the very limited human model result. But we can claim that this drug is a reliable for AD patients because there is no doubt in animal model to reduce the Cholesterol, cognitive impairment and amyloid beta that is a key cofactor of Alzheimer's disease. Also, female survivors of breast cancer have a lower risk of Alzheimer's disease (AD). Thus, cancer Drugs are not a miracle cure for AD- dozens of questions have been raised, however, Bexarotene (chemotherapy) improves cognition and other symptoms that appear with AD patients and will be a significant drug in the coming decades.

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