



Chemotherapy in the elderly: are their needs being met?

The aging of society and the resultant increased numbers of older cancer patients has made the study of this expanding population a priority. Traditionally, older cancer patients have been excluded from clinical trials. The reasons are multiple but include fear of toxicity, low institutional priority, restrictive inclusion criteria, social support and funding issues. The result has been that there is very little prospective data to make evidence-based decisions. This makes the elderly an underserved population with many unmet needs. This is particularly true of patients over 80 years of age for whom virtually no data exists. To date, there have been few studies that have shown a significant difference in the pharmacokinetics between the 'typical' patients and the elderly. Pharmacokinetic differences, when present, have not been clinically relevant. This lack of data mandates trials specific for the elderly. Suggestions for clinical trial design are presented.

KEYWORDS: ageism ■ aging ■ cancer ■ chemotherapy ■ clinical trials ■ comorbidity ■ elderly ■ pharmacokinetics ■ pharmacology ■ polypharmacy

Stuart M Lichtman

65+ Clinical Geriatrics
Program, Memorial
Sloan-Kettering Cancer Center,
650 Commack Road,
Commack, NY 11725, USA
Tel.: +1 631 623 4100
Fax: +1 631 864 3827
lichtmas@mskcc.org

The older cancer patients have not traditionally been the subject of clinical drug development [1]. They are, however, the largest consumers of chemotherapy, and their numbers are rising dramatically. Persons over the age of 65 years are the fastest growing segment of the US population, and will account for an estimated 20% of Americans by the year 2030. Increasing age is directly associated with increasing rates of cancer, corresponding to an 11-fold greater incidence in persons over the age of 65 years versus those under 65 years of age. Consequently, the older population comprises a majority of cancer patients. Despite the increasing incidence of cancer with aging and the aging of the population, only a relatively small number of elderly patients have been entered onto clinical trials [2-4]. Because of this, there is a lack of high-quality data for the clinician to make meaningful decisions. They have, as a result, been underserved in the area of drug development, and undertreated even when data exists regarding efficacious treatment [5,6]. Therefore, the needs of the older cancer patient are not being met. Many trials and retrospective evaluations use the age of 65 years as a cut-off to categorize patients as older or elderly. This is clearly arbitrary, and has been historically used because this is the age of Medicare eligibility. A more clinically relevant breakpoint is in the 70-75-year-old age group where comorbidity, dependency and geriatric syndromes become more prevalent. This article

will focus on pharmacology and issues of drug development pertaining to the elderly, with suggestions regarding drug evaluation.

A number of barriers have been identified that limit the participation of elderly patients in clinical trials [7,8] (Box 1). Cognitive dysfunction is particularly important in understanding the complicated informed consent documents. Cognitive impairments can be as high as 36% in adults aged 85 years and older [9]. Failure of clinicians to offer a clinical trial to eligible older patients is a significant barrier to enrollment [8].

Aging & cancer chemotherapy

Aging is a multidimensional process that is highly individualized, and chronologic age does not always predict the physiological decline in an individual. These effects are due in part to the interaction of comorbidity on aging. It has been suggested that the process of aging is a functional continuum with frailty at the midpoint of independence and predeath [10]. In the primary health stage, there are no significant limitations in activity and minimally reduced functional reserve. Many individuals then become somewhat more vulnerable, with functional reserve critically reduced, causing some functional limitations. The reversibility of some conditions is still possible. The stage of frailty is characterized by severe limitations with no significant recovery of functional reserve [11-14]. Therefore, a goal of assessment is the determination of the

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Box 1. Barriers to participation in trials.

- Focus on aggressive therapy that can be unacceptably toxic in the elderly
- Comorbidity
- Fewer trials available
- Limited expectation of benefit from patient, physicians and family
- Lack of financial and social supports
- Trials have not specifically addressed older or vulnerable adults
- Patient and physician reluctance to include older patients; physicians not recommending therapy, particularly clinical trials
- Social supports
- Insurance
- Mistrust of clinical trials (i.e., guinea-pig syndrome)
- Competition of alternative and complementary therapy

physiologic age of the patient [15]. There is no one precise method of determination, but a comprehensive geriatric assessment or variant is helpful. Part of this assessment is an evaluation of dependency in activities of daily living (ADL) or instrumental activities of daily living (IADL). An assessment of comorbidity, end-organ dysfunction, presence of geriatric syndromes and whether the patient can be defined as frail is critical to treatment planning, particularly the avoidance of treatment-related toxicity. Patients who have deficiencies in one of more of these areas are often appropriately recommended supportive care. Patients in these categories can be thought of as physiologically old. This is particularly true in settings where the benefits of chemotherapy are minimal either in terms of efficacy or palliation (i.e., metastatic pancreatic cancer). It is somewhat more difficult in situations where response to therapy is common. Responses can benefit patients by palliating symptoms. The word cure is often nebulous, particularly in situations where there is significant physiologic decline and the patient's life expectancy is severely limited due to non-cancer-related issues. Adjuvant therapy decisions in older patients with impairments is difficult due to the imprecise prediction of benefit in an individual patient. This has to be weighted against the imprecise prediction of adverse events.

After drugs have been approved at doses applicable to patients with an adequate performance status, studies should be considered in frail and vulnerable populations to determine whether lower doses can be given safely and possibly be used in a palliative setting.

Clinical pharmacology

There are a number of physiological changes that accompany human aging. These include increase in body fat, decrease in lean body mass and decrease in total body water [16–19]. A number of changes in the digestive system can affect

drug absorption. These parameters include decreased gastrointestinal motility, decreased splanchnic blood flow, decreased secretion of digestive enzymes and mucosal atrophy [20,21]. All these factors can result in reduced absorption rate (i.e., in the amount of drug absorbed in the unit of time). Drug compliance is an important issue, particularly with the marked increase in oral anticancer therapies that compound the problem of polypharmacy [22–26].

The volume of distribution (Vd) of drugs is a function of body composition and the concentration of circulating plasma proteins, for example, serum albumin, red blood cell concentration and so on [21,27,28]. Fat content doubles in the elderly from 15 to 30% of body weight, and intracellular water decreases from 42 to 33% in the average 25-year-old compared with the average 75-year-old. These findings emphasize that obesity is a significant problem in the elderly and should be considered in trials [29]. The Cancer and Leukemia Group B evaluated the effect of obesity in patients receiving adjuvant treatment for breast cancer. They found that patients treated within 5% of their actual weight did not experience excessive toxicity. They therefore recommended that initial doses be computed according to actual body weight [30]. This is similar to other malignancies [31]. Hypoalbuminemia and anemia are known adverse prognostic factors in the elderly in both functional ability and survival [32–35].

Age-related declines in the cytochrome P450 has been demonstrated in animal studies and some human trials, but has been inconsistent. Other variables to be considered are the effect of age and diet and genetic polymorphisms [36]. Prospective evaluation of age-related changes in genetic polymorphisms has not been carried out. Many alterations of the enzyme activity involve either drug-induced increases or decreases in metabolism. The biliary excretion of drugs has been studied, but no age-related alterations have been noted [37]. Polypharmacy can also affect metabolism due to the potential of drug–drug interactions [6].

There are also age-related changes in excretory function. There is a gradual loss in renal mass and decline in function with age. This loss is primarily due to loss of cortical mass with relative preservation of the renal medulla. Glomerular sclerosis produces loss of capacity to perform ultrafiltration of plasma, which leads to a decrease in the glomerular filtration rate (GFR) by approximately 1 ml/min for every year over 40 years of age [38–40]. The reduction in GFR is

not reflected by an increase in serum creatinine levels because of the simultaneous loss of muscle mass that occurs with age. In order to facilitate the estimation of glomerular clearance, various equations have been evaluated to calculate creatinine clearance based on the serum creatinine and other factors. Two common equations used clinically are the Cockcroft–Gault and Jelliffe equations [41,42]. The equations are less accurate in populations such as patients with severe renal failure, patients with decreased muscle mass and the elderly. Many individuals lose muscle mass with age. Many elderly individuals with a low serum creatinine of less than 1 mg/dl may actually have diminished muscle mass and diminished production of creatinine, rather than exceptional renal function. A comparison of the accuracy of various formulae has been performed [43]. Dosing modifications for these physiologic declines have been suggested [44–46]. It should be noted that many older patients who have a serum creatinine in the normal range for a particular laboratory have renal insufficiency [47]. Dosing recommendations for older patients and those with renal insufficiency have been published [47–51]. There have been a number of reviews of chemotherapy treatment in older patients that include dosing recommendations [52–54].

Comorbidity & functional status

Comorbidity is a key factor in the overall survival of patients, and therefore the benefits and toxicity of therapy. The role of comorbidity and survival was evaluated by Charlson *et al.* who determined that the number and severity of comorbid illness can predict survival in general medical patients admitted to an inpatient unit [55]. Although disease stage is a crucial determinant of survival, comorbidity increases the complexity of management and affects survival duration [56]. Satariano and Ragland assessed the effect of comorbidity and stage of disease on 3-year survival in women with primary breast cancer [57]. Comorbidity in patients with breast cancer appears to be a strong predictor of 3-year survival, independent of the effects of breast cancer stage. Functional status is also a significant issue in the elderly [58]. Comorbidity and functional status are independent in older cancer patients, and therefore need to be assessed independently. The traditional oncology measures, such as the Karnofsky score and Eastern Cooperative Oncology Group (ECOG) performance scale, may not uncover problems that would be appreciated with the use of a geriatric-specific assessment. Examples include

polypharmacy, social supports, use of the telephone and depression. The degree of dependency and geriatric functional scores can predict survival in older patients [58–61]. Future drug development will require new and easy administering functional scales for the oncologist. These scales must aid the oncologist in predicting toxicity and outcome [62]. Currently available functional scales are the basic ADL, IADL, stair climbing, and performance-based tests, such as ‘get up and go’ and gait speed [63].

End-organ dysfunction

Patients with end-organ dysfunction are usually excluded from clinical trials, particularly for new drugs. The assessment of patients with end-organ dysfunction is critical to guide physicians in dosing. There have been a number of clinical trials using this study design [64–70]. Traditional clinical trial eligibility needs to be reevaluated. For example, when studying a new drug that is not renally excreted then the serum creatinine and/or creatinine clearance requirements need to be relaxed. It is also still not certain which of the available creatinine clearance formulae is most accurate in older patients [43,51,71]. In the clinic the Cockcroft–Gault equation continues to be the standard. The calculation can influence clinical trial eligibility and affect perceptions of safety.

Design issues

For a summary of design issues, see **Box 2**.

■ End point: survival & cause of death

When new therapies are being developed for older patients, it is important to determine the appropriate end point. Particular care must be taken when overall survival is a study end point. A number of studies determined that cause of death may differ in older versus younger patient populations. In lymphoma trials, deaths attributed to tumor or treatment-related toxicity were

Box 2. Clinical trial design.

- Clinical trials specific for elderly patients.
- Some form of geriatric assessment should be performed.
- Comorbidity should be assessed.
- Studies should emphasize particular aspects of aging – that is, frailty, vulnerable elderly and well elderly.
- Polypharmacy and concomitant medications should be evaluated, particularly those drugs interacting with the cytochrome P450 system.
 - Limited sampling strategies should be employed when appropriate
 - Limit office visits and testing to facilitate compliance to the protocol
 - Compliance and adherence
- Quality-of-life assessment should be included.

similar above and below the age of 60 years. The differences in survival were due to other causes of death not obviously related to the lymphoma or its therapy – occurring in 22% of patients greater than or equal to 60 years of age, but only 2% of patients less than 60 years of age ($p = 0.005$). The inclusion of older patients in clinical trials may decrease the overall survival secondary to deaths due to apparently unrelated causes [72,73]. Satariano and Ragland demonstrated that among patients with early-stage breast cancer, there was a fourfold higher rate of all-cause mortality when compared with patients who had no comorbid conditions [57]. This phenomenon is particularly important in cancers that can have a relatively indolent course. In prostate cancer studies it has been shown that competing causes of death are substantive contributors to mortality [74,75]. Progression-free survival, time without symptoms, measuring treatment-free intervals or maintenance of independence (or preventing dependency) may be more meaningful.

■ End point: quality of life

Quality of life is a potentially clinically important end point in clinical trials. In elderly patients, where treatment is often palliative, this is a particularly significant concern. Patient quality of life is affected by a number of factors, related to the disease and treatment characteristics. Quality of life should be as important an objective as survival. Geriatric assessment has also become an integral part of evaluating elderly patients [76,77]. There are many parallels between geriatric assessment and quality of life assessment, in that they are multidimensional and broad. They share many dimensions and focus on issues that are among the most important to older persons, particularly the ability to function fully in social roles and participate in various activities. The compression of morbidity and disability to maximize the preservation of active life expectancy is also a potential end point, particularly in a palliative care setting [78,79].

■ End point: function & clinical benefit

Response rate is one of the standard end points of Phase II studies, and survival and disease-free survival are the standard end points of Phase III studies. In addition, assessment of clinical benefits has become an important end point, especially in the management of metastatic disease, and some agents, including gemcitabine for pancreatic cancer [80] and mitoxantrone for

prostate cancer [81,82], have been approved for use thanks to demonstrated clinical benefits. In the elderly, impaired functional status is a risk factor for disease, and serial measurements in functional status are a potential end point of clinical trials. This was explored in the clinical investigation of infectious syndromes in the elderly. Function was used as a risk factor for infectious syndromes and as an outcome measure [83].

In older individuals with limited life-expectancies, improvement in survival may be difficult to demonstrate and clinical benefits may become paramount. In addition to improvement in pain and other symptoms, the benefits of chemotherapy may include prevention of functional dependence and of functional deterioration. As this is one of the most common complications of diseases in older individuals, it is surprising that it has not been commonly explored as an outcome of cancer treatment. One should add that chemotherapy may not only affect functional status in metastatic incurable cancer, but may also result in changes of functional status in patients whose cancer may be curable, such as patients with breast or colorectal cancer receiving adjuvant chemotherapy and patients with lymphoma. While not usually part of clinical trials, the issues of survivorship in elderly survivors of cancer need to be explored [84–86]. As a result of the increased utilization of screening and earlier detection of common cancers (i.e., breast, colorectal and prostate), coupled with incremental improvements in cancer treatment and supportive care, the number of cancer survivors in the USA has increased from approximately 3 million in 1970 to almost 11 million in 2004. Survivorship has become a separate but related discipline of oncology that requires expertise and the infrastructure to provide optimal care for cancer survivors. Cancer survivors have unique problems. They have their own comorbid issues, often compounded by the residual toxicity of their treatment and the possibility of late adverse effects. There are also emotional issues regarding survivorship. The Institute of Medicine has issued recommendations regarding cancer survivorship programs. A number of centers of excellence have been developed to evaluate different survivorship clinical models. They are focusing on different areas, including behavioral interventions, nutritional interventions, cancer screening, studies of morbidity, physical activity, sexual functioning, fatigue and many other areas.

■ Dose-limiting toxicity

Phase I drug development involves the determination of the dose of chemotherapy to use in subsequent Phase II studies. At each step in the process, the toxicity profile is more accurately defined. Studies of new agents in predetermined stages of aging (i.e., frail, vulnerable) or in patients with specific common comorbidities or functional impairments would be invaluable.

■ Alteration of the dose-limiting toxicity

In certain cases, the dose-limiting toxicity (DLT) may be ameliorated with various interventions. The use of colony-stimulating factors may markedly reduce the period of myelosuppression associated with high doses of cytotoxic chemotherapy, and has increased the therapeutic ratio of standard doses of chemotherapy for elderly patients [87–89]. Hematopoietic support has shifted the focus of DLT from myelosuppression to non-hematologic toxicity. Examples of this include diarrhea with irinotecan and neuropathy with oxaliplatin. The elderly patient may have a different spectrum of DLT than a younger patient. Schedule and formulation changes may allow potentially toxic agents to be used in the elderly population. The common toxicity criteria as currently used may not be adequate to assess adverse events in elderly patients. For example, assessment of neuropathy should include evaluation of functional decline or falls. The reporting of clinical trials should also be elder-specific. Most trials only report grade III/IV toxicity; grade II toxicity in an older patient has clinical relevance. It will help clinicians in decision making if they know the full spectrum of toxicity.

There have been a limited number of evaluations involving elderly patients [90]. Traditionally, during the Phase I investigation, acute toxicities are identified and the potential duration and reversibility of the toxicities are defined. While patients with malignancy who have limited therapeutic options may be offered an opportunity to participate in these trials, selection of appropriate patients to accurately evaluate toxicity in a Phase I clinical investigation is extremely important [91]. In general, patients should have reasonably good performance status and basically normal organ function. As a result, entry criteria may exclude elderly patients from dose-finding trials. Studies in the elderly can be defined differently from what has historically been done. Variations in performance and functional status can be defined in the eligibility. If such a study is performed, the final dose that is

determined will be applicable to that particular group of patients. The heterogeneity of the elderly limits the value of drug studies carried out in fit, younger patients. End points may be different because of age-related changes in organ function as previously discussed, or secondary to comorbid conditions. Organ dysfunction studies can be performed in both younger and older patients to define the dose in each population.

Polypharmacy is quite frequent in the older population. The number and type of concomitant medications need to be carefully assessed when patients are entered into clinical trials. Older ambulatory patients use threefold more medications than younger patients [36]. At least 90% of the older patients used at least one medication, and the average is at approximately eight medications per patient [92]. Self-medication with herbal remedies and other alternative therapies are becoming increasingly common. Significant drug interactions, particularly those involved in the cytochrome P450 system, are of major concern [93–95]. Polypharmacy may limit older patient participation in trials, particularly those with pharmacokinetic analyses and end points. These studies may exclude patients on a specific medication that may affect the metabolism of the study drug. Pharmacogenetic profiles may also aid in reducing toxicity [6].

■ Sampling

There is a clear need for elderly patients to be involved early in the development of anticancer agents. Pharmacokinetic drug sampling is an integral part of the process. Accuracy of specimen acquisition is critical. To help ensure accurate pharmacological results, the schedule of blood sampling must be carefully considered. Limiting sampling has been applied to many agents [96–105]. A few data points can be used in the approach of population pharmacokinetics [106]. A trial of paclitaxel and aging has used this approach successfully [107]. Limited sampling strategies are particularly important for older patients as it minimizes the number of office visits, which simplifies compliance. Therefore, it also may allow more older patients to participate in dose-finding studies. This would make the results of Phase I trials more applicable to the elderly.

Undertreatment

A review of undertreatment in older female cancer patients discussed breast and gynecologic cancers [5]. It has been amply demonstrated that older women had less breast-conserving surgery,

less axillary node dissection and less radiation therapy or adjuvant chemotherapy. This is despite adequate evidence describing the efficacy of therapy in older women [108]. In ovarian cancer there was less complete debulking surgery and less adjuvant chemotherapy in terms of frequency and dose. This has also been demonstrated in adjuvant colon cancer treatment, in which older patients received less therapy despite proven efficacy of treatment [109,110]. Some reasons for undertreatment include the lack of adequate data for the clinicians. There is also a problem with the dissemination of available information that shows older patients tolerate standard regimens with acceptable toxicity. Older patients tend to be more complex due to their multiple comorbidities, polypharmacy, geriatric syndromes and functional impairments [111–113]. They are therefore more time-consuming to adequately assess, which also contributes. This issue does magnify the need for a simple but predictive assessment to aid the oncologists in decision making, particularly in the realm of adjuvant therapy.

Proposals

The elderly have been underserved and their needs have not been met. The need for information regarding the elderly requires an alternative trial design and evaluation. There are options available that can improve the current situation.

Phase II clinical trials in older individuals appear to be the quicker and most effective way to obtain this information. These trials, including studies of drug bioavailability, compliance and adherence, appear essential for oral agents. Parenteral agents undergoing extensive liver metabolism or renal excretion should be evaluated with varying degrees of organ dysfunction. In these studies, the AUC of the parent compounds and active metabolites should be correlated to toxicity and response rate. In the development of new agents, the conduction of three-arm Phase II randomized studies, including individuals under 65 years of age, those 65–75 years of age and those over 75 years, is an option to establish in an estimate whether the activity and toxicity of these agents is similar in younger and older individuals. In some circumstances, age may be too arbitrary, and a combination of age and functional status may be a more appropriate way to stratify patients. Patients with functional impairment and possibly frailty need to be included.

Functional outcome should be studied in all individuals aged 64 years and older undergoing Phase II, III and IV clinical trials. In addition to

performance status, this should include evaluation of the ADL and IADL and changes in living conditions, whether living alone, with a family, with a friend or in an adult living facility at the beginning and at the end of chemotherapy. In addition, individuals for whom a prolonged survival is expected (adjuvant chemotherapy for breast, colorectal and lung cancer, patients with lymphoma) should undergo yearly assessment of function and living conditions, as well as of comorbidity. Serial functional assessment will be valuable in combined modality trials, particularly utilizing surgery and radiation [114]. It may be that therapy may increase the incidence of comorbid conditions, including coronary artery disease, congestive heart failure, chronic pulmonary disease, hypertension and diabetes. Therapy can exacerbate pre-existing comorbidities. Together with function, comorbidity is one of the most important determinants of survival and independence in older individuals [115]. The abbreviated assessment now currently under development will be particularly useful in this regard. Journal editors should encourage the inclusion of age-related analyses in the reporting of clinical trials to provide meaningful information for clinicians caring for older patients

Phase I trials are a special issue for the elderly. While no-one should be excluded from Phase I trials on account of their age, we also feel that a special effort to increase the enrollment of older individuals in these trials may be ill considered. The inclusions of individuals with multiple comorbidities in these trials may delay the development of new drugs, as it may exaggerate the risk of complications and may lead to maximum tolerated doses that are too low to be effective. The performance of Phase II trials specifically designed for older individuals, with correlative pharmacokinetics, appears to be the most practical way to obtain the information needed.

The involvement of older individuals in trials of adjuvant treatment represents a special problem. Clearly, in a population with reduced life-expectancy, the benefits of chemotherapy appear lessened and the risk increased. A number of programs allow the calculation of individual benefits of cancer chemotherapy based on life-expectancy and risk of recurrence [116]. Due to the small contribution of older patients in these algorithms, the results with regard to the older cancer patient need to be evaluated in that light. It is reasonable to use them as frame of reference to make clinical decisions.

Conclusion

The elderly are a medically underserved population with many unmet needs. This is particularly true of the area of cancer treatment. As they have not been part of a significant amount of clinical trials, there is little data on which to base clinical decisions. This is particularly true of the vulnerable elderly. These are individuals with significant comorbidity and functional decline in whom data regarding the use of chemotherapy is virtually nonexistent. Therefore, clinicians have to extrapolate from data accumulated in a younger, healthy population. These can result in undertreatment with poorer outcomes or excessive toxicity. There is a need for a quick, simple and predictive tool for assessment of these individuals. This is currently undergoing investigation. Clinical trial designs need to be altered to meet the needs of the elderly. These design issues need to alter our concept of clinical benefit, toxicity evaluation and assessment. As the elderly become the predominant population of cancer patients, they need to become the focus of our endeavors.

Future perspective

In the next decade, the 'baby boomers' will age and older cancer patients will predominate. At that point, our ability to accurately assess the older patients will improve so that predictions of toxicity and benefit will be much more precise. It is hoped that in the area of drug development

the particular problems of older individuals will be recognized and incorporated into clinical trial design. Prospective evaluation of new drugs and new drug combinations will be evaluated in older individuals, many of whom will have significant comorbidity and functional impairments. This will make the data generated more applicable to the general population of patients. Pharmacokinetic analysis will be routine, and each drug will be tested in patients with varying degrees of end-organ dysfunction. The common toxicity criteria will be adjusted to more accurately evaluate the toxicities particular to the elderly. Older patients will be encouraged to enter clinical trials, and this may need to be incentivized through Medicare. As oral therapy continues to become more common, issues regarding polypharmacy and drug interactions will be studied further to avoid adverse drug events and increased toxicity. The longitudinal effects of treatment will be studied and a survivorship plan will be integral to the treatment.

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Executive summary

Introduction

- There is a paucity of clinical trial evidence for the elderly and there are many barriers to clinical trial participation.

Clinical pharmacology

- There are few clinically relevant pharmacokinetic changes based on age alone. Changes that are observed are due to end-organ dysfunction, most notably renal dysfunction.

Comorbidity & functional status

- Assessment of comorbidity is a significant part of the patient's assessment.
- The evaluation of patients with poor performance scores and/or functional disability will be important in determining treatment plans. Function will emerge as the critical variable in the treatment of older patients, and will be assessed much more commonly than it is now.

End-organ dysfunction

- As patient's age, there is increased end-organ dysfunction. This is a result of the aging and comorbidity. In general, there are no age-related pharmacokinetic changes. The pharmacodynamics changes noted are specifically for the drug studied. There have been many publications addressing the issue of drug studies in patients with abnormal renal function and other disabilities. This has provided a wealth of information.

Clinical trial design

- Various aspects of clinical trials need to be observed. Clinical trials specific for elderly patients need to be developed. It should include geriatric assessment.

Undertreatment

- Due to the lack of meaningful data, older patients tend to have poor treatment plans and outcomes. This phenomenon is well documented. Clinicians will need to carry out a geriatric assessment, which will be invaluable for treatment planning.

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