

PERSNIEUWS

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Overlevingsduur bij ernstige niercelkanker verlengd door nieuwe behandelmogelijkheid Torisel

Overlevingsduur significant verlengd voor niercelkanker patiënt met uitzaaiingen en slechte prognose

In Nederland komen jaarlijks ruim 1500 nieuwe gevallen van niercelkanker voor. In de meeste gevallen is de ziekte uiteindelijk dodelijk. Behandeling richt zich op levensverlenging plus het verhogen van de levenskwaliteit en is zowel fysiek als mentaal zwaar. Daar komt bij dat voor geen van de tot nu toe beschikbare behandelopties verlenging van de overlevingsduur is bewezen.

Voor niercelkanker werkt Torisel als eerste middel via het zogenaamde mTOR-pathway. Dat wil zeggen dat Torisel zich direct richt op het eiwit in de cel met een centrale rol bij processen zoals de celdeling (celproliferatie) en de nieuwe bloedvatvorming onder andere in tumoren (angiogenese). Torisel remt deze processen. De behandeling met Torisel heeft voor het eerst een verlenging op de overlevingsduur bij niercelkanker aangetoond. Voor niercelkanker patiënten met uitzaaiingen en een slechte prognose, is bewezen dat met Torisel zowel de levensduur (overall survival) als de termijn dat de ziekte niet verergert (progression-free survival) significant toenemen.

Overleving met maanden verlengd

Onderzoek in vergelijking met een bestaand middel (interferon-alfa) heeft aangetoond dat de gemiddelde overlevingsduur (overall survival) van patiënten met uitgezaaide niercelkanker en een slechte prognose door Torisel met bijna de helft toeneemt (10,9 maanden versus 7,3 maanden bij interferon-alfa). Daarnaast wordt bij deze patiënten de termijn dat de ziekte niet verergert (progression-free survival) significant verlengd (5,6 maanden versus 3,2 maanden bij interferon-alfa).

"Torisel is een belangrijke aanwinst voor de behandeling van patiënten met uitgezaaide niercelkanker. De verlenging van de overleving met Torisel is van groot belang. Het nieuwe werkingsmechanisme spreekt mij in het bijzonder aan", aldus Bob Pinedo. Als gedreven behandelaar van patiënten, staat de wetenschappelijke carrière van Prof. dr. Pinedo in het teken van het werkingsmechanisme van anti-kankermiddelen. Pinedo is tevens initiatiefnemer van het Cancer Center Amsterdam. Zijn werk is met verschillende internationaal toonaangevende prijzen onderscheiden.

Toepassingen en verder onderzoek

In Nederland vormen patiënten met uitgezaaide niercelkanker en een slechte prognose ongeveer éénderde deel van het totaal aantal patiënten met niercelkanker.

Als eerste zijn voor Torisel specifieke onderzoeksdata beschikbaar in een grote groep patiënten met niercelkanker en een slechte prognose. De Europese Commissie heeft Torisel in november 2007 goedgekeurd als eerste aangewezen behandeling (eerstelijns) voor uitgezaaide niercelkanker met een slechte prognose. Voor niercelkankerpatiënten met uitzaaiingen en een

gemiddelde of goede prognose zal Torisel als tweedelijns behandeling of in combinatie met een bestaande behandelmogelijkheid worden onderzocht. Verder is de positieve werking van het mTOR-mechanisme van Torisel ook op andere vormen van kanker in onderzoek.

Torisel en Wyeth

Torisel (stofnaam temsirolimus) wordt op de markt gebracht door Wyeth Pharmaceuticals bv te Hoofddorp. Momenteel worden de professionals geïnformeerd die bij de behandeling van niercelkanker betrokken zijn zoals urologen en oncologen.

Wyeth Pharmaceuticals bv is onderdeel van Wyeth, één van de meest vooraanstaande ontwikkelaars en makers van receptgeneesmiddelen, vaccins, vrij verkrijgbare geneesmiddelen en veterinaire preparaten.

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Bijlagen:

1) Newsrelease Wyeth: 'Wyeth's Torisel receives European Commission approval for the treatment of advanced kidney cancer'

2) Graphic Wyeth (vrij van rechten): De werking van het mTOR inhibitor Torisel

Bijlage 1

Wyeth's TORISEL Receives European Commission Approval for the Treatment of Advanced Kidney Cancer

TORISEL Extends Median Overall Survival vs. Interferon-Alpha

Collegeville, Pa., November 26, 2007 – Wyeth Pharmaceuticals, a division of Wyeth (NYSE:WYE), announced today that the European Commission has approved TORISEL™ (temsirolimus) for the first-line treatment of patients with advanced renal cell carcinoma (RCC) who have at least three of six prognostic risk factors. TORISEL is the only approved cancer therapy that specifically inhibits the mTOR (mammalian target of rapamycin) kinase, an important regulator of cell proliferation, cell growth and cell survival. TORISEL was approved in the United States in May 2007 for the treatment of advanced RCC.

Renal cell carcinoma accounts for approximately 85 percent of the estimated 85,000 new cases of kidney cancer diagnosed in Europe annually. TORISEL is the only renal cancer therapy proved to extend median overall survival compared with interferon-alpha in patients with advanced RCC.

“Temsiroliimus was studied in the most difficult-to-treat patients with advanced renal cell carcinoma: those who have multiple risk factors that have been associated with shortened survival,” says Bernard Escudier, M.D., Head of the Immunotherapy Unit, Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, and an investigator in the TORISEL phase 3 study. “The ability of temsirolimus to provide an increase in overall survival in these patients provides us with a much-needed new option for the treatment of advanced kidney cancer.”

TORISEL was studied in a three-arm, Phase 3 clinical trial of 626 patients with advanced RCC and three or more of six preselected prognostic risk factors who had received no prior systemic therapy. In the study, TORISEL significantly increased median overall survival by 49 percent compared with interferon-alpha (10.9 months vs. 7.3 months, $P=0.0078$). TORISEL also was associated with a statistically significant improvement over interferon-alpha in the secondary endpoint of progression-free survival (when the disease does not worsen; 5.6 months vs. 3.2 months, $P=0.0042$). The combination of TORISEL and interferon-alpha did not result in a significant increase in overall survival when compared with interferon-alpha alone.

“The European Commission’s approval of TORISEL underscores the importance of this therapy for patients with advanced kidney cancer and reinforces the potential of this mechanism of action as a new approach in oncology,” says Robert R. Ruffolo, Jr., Ph.D., President, Wyeth Research, and Senior Vice President, Wyeth.

About TORISEL

TORISEL is an mTOR inhibitor indicated in the European Union for the first-line treatment of patients with advanced RCC who have at least three of six prognostic risk factors. These risk factors include less than one year from time of initial RCC diagnosis to randomization, Karnofsky performance status of 60 or 70, hemoglobin less than the lower limit of normal, corrected calcium of greater than 10 mg/dL, lactate dehydrogenase >1.5 times the upper limit

of normal and more than one metastatic organ site. In the United States, TORISEL is indicated for the treatment of advanced RCC.

Inhibition of mTOR in treated cancer cells blocked the translation of genes that regulate the cell cycle. In in vitro studies using renal cancer cell lines, TORISEL inhibited the activity of mTOR and resulted in reduced levels of certain cell growth factors involved in the development of new blood vessels, such as vascular endothelial growth factor.

In March 2007, the European Association of Urology published guidelines recommending that TORISEL be considered as first-line treatment in patients with advanced RCC with poor-risk features. In August 2007, the National Comprehensive Cancer Network (NCCN) in the United States added TORISEL to the NCCN Kidney Cancer Guidelines as an option in first-line therapy for both predominant clear cell histology and non-clear cell histology and as a subsequent therapy option for patients with predominant clear cell histology.

TORISEL U.S. Important Safety Information

Hypersensitivity reactions manifested by symptoms, including, but not limited to anaphylaxis, dyspnea, flushing and chest pain have been observed with TORISEL.

Serum glucose, serum cholesterol and triglycerides should be tested before and during treatment with TORISEL.

The use of TORISEL is likely to result in hyperglycemia and hyperlipemia. This may result in the need for an increase in the dose of, or initiation of, insulin and/or oral hypoglycemic agent therapy and/or lipid-lowering agents, respectively.

The use of TORISEL may result in immunosuppression. Patients should be carefully observed for the occurrence of infections, including opportunistic infections.

Cases of interstitial lung disease, some resulting in death, have occurred. Some patients were asymptomatic and others presented with symptoms. Some patients required discontinuation of TORISEL and/or treatment with corticosteroids and/or antibiotics.

Cases of fatal bowel perforation occurred with TORISEL. These patients presented with fever, abdominal pain, metabolic acidosis, bloody stools, diarrhea and/or acute abdomen.

Cases of rapidly progressive and sometimes fatal acute renal failure not clearly related to disease progression occurred in patients who received TORISEL.

Due to abnormal wound healing, use TORISEL with caution in the perioperative period.

Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

Live vaccinations and close contact with those who received live vaccines should be avoided.

Patients and their partners should be advised to avoid pregnancy throughout treatment and for 3 months after TORISEL therapy has stopped.

The most common (incidence $\geq 30\%$) adverse reactions observed with TORISEL are: rash (47%), asthenia (51%), mucositis (41%), nausea (37%), edema (35%), and anorexia (32%).

The most common laboratory abnormalities (incidence $\geq 30\%$) are anemia (94%), hyperglycemia (89%), hyperlipemia (87%), hypertriglyceridemia (83%), elevated alkaline phosphatase (68%), elevated serum creatinine (57%), lymphopenia (53%), hypophosphatemia (49%), thrombocytopenia (40%), elevated AST (38%), and leukopenia (32%).

Most common Grades 3/4 adverse events included asthenia (11%), dyspnea (9%), hemoglobin decreased (20%), lymphocytes decreased (16%), glucose increased (16%), phosphorus decreased (18%) and triglycerides increased (44%).

Strong inducers of CYP3A4/5 (e.g., dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.

St. John's Wort may decrease TORISEL plasma concentrations, and grapefruit juice may increase plasma concentrations of the major metabolite of TORISEL, and therefore both should be avoided.

The combination of TORISEL and sunitinib resulted in dose-limiting toxicity (Grade 3/4 erythematous maculopapular rash and gout/cellulitis requiring hospitalization).

Please see TORISEL full U.S. Prescribing Information at <http://www.TORISEL.com>.

Wyeth Pharmaceuticals

Wyeth Pharmaceuticals, a division of Wyeth, has leading products in the areas of women's health care, infectious disease, gastrointestinal health, central nervous system, inflammation, transplantation, hemophilia, oncology, vaccines and nutritional products.

Wyeth is one of the world's largest research-driven pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing and marketing of pharmaceutical, vaccines, biotechnology products and non-prescription medicines that improve the quality of life for people worldwide. The Company's major divisions include Wyeth Pharmaceuticals, Wyeth Consumer Healthcare and Fort Dodge Animal Health.

The statements in this press release that are not historical facts are forward-looking statements based on current expectations of future events and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. These risks and uncertainties include the inherent uncertainty of the timing and success of, and expense associated with, research, development, regulatory approval and commercialization of our products, including with respect to our pipeline products; government cost-containment initiatives; restrictions on third-party payments for our products; substantial competition in our industry, including from branded and generic products; data generated on our products; the importance of strong performance from our principal products and our anticipated new product introductions; the highly regulated nature of our business; product liability, intellectual property and other litigation risks and environmental liabilities; uncertainty regarding our intellectual property rights and those of others; difficulties associated with, and regulatory compliance with respect to, manufacturing of our products; risks associated with our strategic relationships; economic conditions including interest and currency exchange rate fluctuations; changes in generally accepted accounting principles; trade buying patterns; the impact of legislation and regulatory

compliance; risks and uncertainties associated with global operations and sales; and other risks and uncertainties, including those detailed from time to time in our periodic reports filed with the Securities and Exchange Commission, including our current reports on Form 8-K, quarterly reports on Form 10-Q and annual report on Form 10-K, particularly the discussion under the caption "Item 1A, RISK FACTORS." The forward-looking statements in this press release are qualified by these risk factors. We assume no obligation to publicly update any forward-looking statements, whether as a result of new information, future developments or otherwise.

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