Trends-in-Medicine

January 2005
By Lynne Peterson

SUMMARY
Surprisingly, Shire was not at this meeting and not promoting its new phosphate binder, Fosrenol. ♦ Nephrologists do not believe their use of EPO will be affected by Medicare reimbursement cuts. ♦ Use of Amgen's Sensipar is growing, with no effect on Genzyme's Renagel or vitamin D, but doctors expect to cut vitamin D use by as much as half in the future. ♦ FibroGen's FG-2216, an oral erythropoiesis stimulator which is starting Phase II trials, generated some buzz. ♦ There was no excitement about Keryx's sulodexide, but it looks promising for treating diabetic neuropathy. ♦ Davita's purchase of Gambro is viewed positively; Davita is considered much better run than Gambro, and the joint company will have more bargaining power, but the challenge will be meshing two very different cultures. ♦ Use is increasing of Bone Care International's IV and oral Hectoral, but Abbott may stop or reverse any share loss when it gets approval for oral Zemplar.

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RENAL RESEARCH INSTITUTE'S 7TH INTERNATIONAL CONFERENCE ON DIALYSIS

January 19-21, 2005
New Orleans

End stage renal disease (ESRD) has increased over the past 30 years much faster than experts expected. By 2030, experts now believe there will be two million people on renal dialysis, up from 400,000 today, accounting for 3% of the entire Medicare population and as much as 20% of Medicare expenditures.

An NIH official offered some interesting factoids about ESRD:

- First year graft survival increased from ~62% in 1978 to ~90% in 2001.
- In 2002, 85% of patients received adequate dialysis – 89% of white patients and 83% of African-Americans. This compares to 43% overall in 1993.
- ESRD program expenditures in 2001 were ~$4 billion for inpatients and another $6 billion for outpatients.
- Per capita Medicare ESRD expenditures averaged $44,754 in 2002, which compares to $5,682 for the average Medicare patient that year. He said, "ESRD is still a very expensive patient population, but one can make a strong argument that ESRD is exceedingly cost-effective and cost-controlling over time."

The home dialysis market is holding fairly steady at a small percent of dialysis patients, but peritoneal dialysis (PD) is growing a little. A Michigan doctor said, "We are trying to convince our younger pre-dialysis patients to consider PD, but they are afraid of it, afraid that they can't do it properly. Acceptance of PD depends on the patient's education level; the higher the education level, the more open a patient is to PD." The medical director of Kaiser Permanente's ESRD program said, "I'm a big proponent of home dialysis, but we only have eight patients (out of ~3,500) on home dialysis now. We started the first pilot program last year, and we hope to get several more going this year. I think it will catch on because it is the right thing for the patient, there is a dialysis nurse shortage, and we can save money with home dialysis." An industry official said, "PD maintains better quality of life, but many doctors argue it is temporary (two to four years, on average). That's why they don't push it. Use would increase if it were driven by managed care."

Kaiser Permanente also is trying to spur usage of PD. The medical director said, "Currently about 11% of our dialysis patients are on PD. We will focus on that this year. PD costs $20,000 per patient per year less than in a dialysis unit. But it requires a culture shift, and we are focusing on new patients, saying they should do PD, and if they can't, then they should do home dialysis. In-center dialysis will be a last resort. By next year, I expect 13%-14% of our patients to be on PD, and 20% to be on PD in two years. Eventually, we would like to get to 30% on PD."

Nephrologists agree there are benefits to treating patients earlier, before dialysis, when they have CKD, but the problem is twofold: (1) Primary care physicians are not referring patients early enough, and (2) Medicare reimbursement is not sufficient. A source explained, "If Medicare said it would pay for CKD, we would see more patients. Right now, Medicare only pays for dieticians. Paying the nephrologist would be the tipping point. Otherwise, CKD treatment has to be health-plan initiated." A CMS official doubted that Medicare will cover CKD in the near future, saying, "A number of us are advocating addressing the ESRD program to include CKD, but that would probably require legislative action." Another expert said, "We have to get primary care doctors to refer patients. That is the breakdown in the CKD program."

ANEMIA

The federal government appears as committed to eliminating erythropoietin (EPO) as a profit source for dialysis clinics as they are in removing oncologists' profit on chemotherapy drugs. As one expert explained:

- **2004.** "Medicare paid $10 per 1,000 units, regardless of the price we paid. So, for 5,000 units we got $50.00."
- **2005.** "On a quarter-by-quarter basis, Medicare will pay, based on the flat ASP. Right now, it means $9.76 per 1,000 units. For 5,000 units it is $48.80 + $0.50 as the administration fee, for a total of $49.30. This means a $0.70 reduction in payments for each 5,000 units."

Yet, despite this downward pressure on EPO profitability, most nephrologists did not think their use of EPO would decrease. A doctor said, "We have to follow the K/DOQI guidelines even if it is not profitable." Another commented, "EPO reimbursement won't affect my use…EPO is a wonder drug, so a reimbursement change will not change use." A New York doctor said, "If CMS is going to have a quality of care reward system, you couldn't do that (cut back on EPO use)." Another source said, "CMS will be watching to see if clinics reduce their use of EPO too much because of the reimbursement changes."

Instead, what may happen, some doctors predicted, is that:

- **Less hemoglobin testing.** Centers which were testing hemoglobin more frequently than the once-a-month required by Medicare might cut back to just monthly testing.
- **Home administration.** Dialysis patients may be told to self-administer the EPO subcutaneously at home.
- **Sliding scale adjustments or titration schedules.** A Florida doctor said, "The sliding EPO scale could be revised if EPO reimbursement gets too unprofitable because I won't stay in business if I can't get reimbursed."

Sources generally do not believe that EPO – Amgen's Epogen and Aranesp (darbepoetin alpha) or Johnson & Johnson's Procrit – is either over-utilized or under-utilized. A nurse practitioner said, "There is no over-utilization of EPO. Every month we critically review all our EPO use." An industry official said, "Those companies over-shooting the K/DOQI guidelines will cutback on their EPO use, but not until all the profit is out. I think there is a little profit there still."

Some doctors suggested there is not enough EPO use in pre-dialysis patients. A Midwest doctor commented, "A lot of primary care doctors are not addressing too low hemoglobin, and they let patients have low hemoglobin too long. Very, very few CKD patients are being treated (for low hemoglobin). That is a huge market." A California doctor explained one of the problems: "Nephrologists are not paid for CKD consults or visits. Optimal Renal Care (a disease management company), for example, is being hired by health plans more and more to manage CKD. So more patients may get referred to nephrologists because of disease management companies."

AMGEN'S Aranesp (darbepoetin alpha)

Sources said they are using little or no Aranesp in CKD patients because of cost. A California nephrologist said, "There is no big advantage to Aranesp. We have >500 patients who self-administer Procrit at home. We tried Aranesp and didn't think the results were different, and it was more expensive." Another doctor said, "Aranesp is used in a lot of hospital dialysis facilities because hospital pharmacies can negotiate a lower price, but it is not generally used in outpatients because of cost."

FIBROGEN'S FG-2216

FG-2216 is an inhibitor of HIF-PH, an enzyme that regulates the stability and activity of HIF. It is designed to stabilize HIF and selectively activate the body's natural process of HIF-mediated erythropoiesis, including the induction of endogenous EPO and the mobilization and utilization of iron stores, essential to the formation of new oxygen-carrying red blood cells. FibroGen licensed FG-2216 to Yamanouchi Pharmaceutical Co. for development and sale in Japan for the treatment of anemia, but FibroGen retained the rights for the rest of the world.

There was some buzz in the nephrology community about this oral, small molecule erythropoiesis stimulator, even though the drug has only be studied in Phase I trials. In Phase I, FG-2216 was dosed two or three times weekly at doses ranging from 0.3-20.0 mg/kg. Adverse events included nausea and headache but were mild and subsided with continued administration.

Numerous sources have heard about FG-2216, and there is a fair amount of interest in it. A New York doctor said, "It is very promising. I haven't heard of any toxicity yet. It could replace EPO first-line." An investigator said, "I think it is promising…It is pretty early, but it is exciting because it is translational research…Whether eventually it will change the treatment of anemia is hard to predict, in particular because the current treatment has an excellent safety record…Clearly, an oral EPO would be an advantage, no doubt, but it has to compete with a well-established treatment."

Several Phase II trials are due to start this year, and an expert predicted the results will be known in two or three years – not 10 years from now. A speaker reviewed the science of HIF-PF inhibitors, saying, "One of the interesting questions that the Phase II trials will answer is whether stimulation of endogenous EPO will work reproducibly in patients with kidney disease…It is possible that you could titrate this as nicely as EPO, or it might be used as a background therapy, with fine tuning with supplemental EPO."

No toxicity has been noted in animal or human clinical trials, and an expert was unaware of any toxicity questions raised by the mechanism of action. He said, "No relevant toxicity was reported in animals, but we probably have to be careful and check broadly because it is systemic with broad implications, so it is not predictable what kind of toxicity might be seen."

Would FG-2216 be useful in anemia of chronic disease? Sources agreed there is a real market opportunity for EPO in anemia of chronic disease, but an expert said FG-2216 may not be as useful in anemia of chronic disease as in renal disease, "You would need a higher dose, and the responses would be less predictable. But there is evidence it works in IBD, etc., where EPO therapy is useful but cost restricts its use."

VITAMIN D ANALOGS: ABBOTT'S Zemplar (paricalcitol) and BONE CARE INTERNATIONAL'S Hectoral (doxerecaliferol)

A speaker suggested that all CKD patients may benefit from some vitamin D, "Vitamin D may be critical to the survival of all patients with CKD." Several doctors said they found this a compelling argument.

Yet, the Department of Justice is investigating several dialysis chains, over either the use of vitamin D analogs – which are a profit center for dialysis clinics – or over the PTH testing used to determine the need for vitamin D supplementation. Sources aren't sure which is the issue – the drug or the test – but most believe it is the use of the vitamin D analogs, that is the real issue. As one doctor put it, "Follow the money. Vitamin D is what's costing the government money, so I'm sure that's what they are looking at." An industry official said, "I ask about this at every meeting, but no one seems to know. I think it revolves around the test." Another expert said, "Monthly PTH measurement does not get you in trouble – if you are making a (dosing) change. If you are not making a change, then quarterly measurements are fine."

The most commonly used PTH test measures intact PTH (iPTH), but Scantibodies offers a whole-PTH test. Doctors were dubious about the value of the Scantibodies test. Experts were more interested in bio-intact PTH (biPTH). One said, "We will adopt biPTH because that is measuring an actual active hormone. The ratio of PTH 1-84/7-84 (the Scantibodies test) has not been validated, is not consistent with large studies showing a high correlation between iPTH and biPTH…I don't use it, I don't recommend it, and I would never dose a patient based on that." Another commented, "The Scantibodies test may be a better test, but does it lead to better outcomes? And the K/DOQI guidelines don't use it."

For dialysis patients, sources said IV Zemplar is much more commonly used than IV Hectoral, but IV Hectoral use is growing, and doctors predicted that trend will continue. For pre-dialysis patients, oral Hectoral has the advantage because no oral Zemplar is available yet. However, once oral Zemplar is approved, sources expect the IV lead-in to help the oral take market share from oral Hectoral. Yet, there is no excitement over oral Zemplar, and several sources described it as a me-too drug. Comments on oral Zemplar included:

- *Connecticut:* "I'm familiar with IV Zemplar in dialysis patients, so it might be easier for Abbott to convert me to Zemplar in pre-dialysis patients if they get an oral Zemplar."
- *North Carolina:* "I'm not excited about oral Zemplar, but what could make it exciting is price."
- *Michigan:* "IV Zemplar has less effect on phosphorous. I'd try oral Zemplar if a patient had high phosphorous."
- *Wisconsin:* "I use both IV Hectoral and IV Zemplar in dialysis patients, and I use oral Hectoral in pre-dialysis patients. Zemplar claims to cause less hypercalcemia, but I'm not sure if that is true with oral Zemplar."
- *Illinois:* "I've started to use oral Hectoral, with an emphasis on pre-dialysis management, and my use is likely to increase."
- *California:* "I use Hectoral because of its ability to transition from IV to oral, but Zemplar will get a boost when oral Zemplar is approved."

If Medicare cuts the profitability of IV vitamin D analogs as well as EPO, clinics and doctors may start using more oral vitamin D analogs. An industry source said, "If there is no profit in the IV, many doctors will push the oral preparations – if the patients can tolerate that."

SECONDARY HYPERPARATHYROIDISM: AMGEN'S Sensipar (cinacalcet)

In March 2004, Sensipar, an oral calcimimetic, was approved by the FDA for the treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis. On average, doctors are currently using Sensipar for <10% of their ESRD patients, but most expect use to increase over the next year, perhaps doubling. So far, Sensipar has not impacted the use of Genzyme's Renagel (sevelamer) or affected the Renagel dose; Sensipar is simply added on top of Renagel. A Midwest doctor said, "We try not to change the Renagel dose."

Most doctors using Sensipar have not cut back their vitamin D usage – yet. Rather, they are adding Sensipar to vitamin D. However, this situation is not expected to continue once doctors get more familiar with Sensipar. Most sources expect to cut vitamin D doses by up to 50% as they get more comfortable with Sensipar. A speaker, asked to talk about how Sensipar affects vitamin D use, said, "I can't answer how Sensipar will impact vitamin D use because the data are not in yet. The studies have not been done to address this…The Phase III trials do not let us answer the question." However, he went on to lay out a rationale for cutting vitamin D use by 50% when Sensipar is prescribed.

Sources agreed that Amgen is treading carefully in its marketing of Sensipar, not wanting to scare doctors away by making them choose between Sensipar and a drug (vitamin D) that makes money for their center. Thus, doctors are adding Sensipar on top of vitamin D for now, but sources said they expect to start reducing their use of vitamin D soon. One said, "I haven't cut the vitamin D yet, but I plan to cut it by 40%."

Longer-term, will Sensipar be used in CKD? Doctors just are not sure yet. Sensipar is too new for them to predict when or how much.

Comments on Sensipar included:

- *North Carolina:* "Companies make money on IV Zemplar now, so telling patients to take something the patient has to pay for, the company can't provide, and the company doesn't make money on doesn't make sense."
- *Michigan:* "Less than 10% of our ESRD patients are on Sensipar now, but in a year it will probably be about 15%. It's a new drug, and people are still getting a feel for it and how to dose it…There is a learning curve with Senispar…We add Sensipar on top of everything; we don't use it first-line yet."
- *Arkansas:* "We are starting to use a little Sensipar, but not first-line. In the last three to four months, we've been talking about it more at meetings. Our use is likely to increase, but if there is even one serious adverse event with Sensipar, that will make us reconsider our use of it."
- *New York:* "So far, I don't have enough experience with Sensipar to see if I can reduce the vitamin D."

PHOSPHATE BINDERS

SHIRE'S Fosrenol (lanthanum)

Nephrologists weren't asking "Where's Waldo?" at the Renal Research dialysis conference, but they were wondering "Where's Shire?" Shire has the newest drug for dialysis patients – Fosrenol, which was approved by the FDA on October 27, 2004 – but the company did not have a booth at this meeting and did not sponsor any seminars or talks on phosphate binding in general or Fosrenol in particular.

Furthermore, the company apparently has been very slow to detail nephrologists about chewable Fosrenol.

- Only two nephrologists questioned had been detailed on Fosrenol. One, who explained that he had been part of the clinical trials for the drug, offered a lukewarm comment, saying, "I haven't written a prescription for it yet, but I probably will use it sometime in the future. Fosrenol, PhosLo (Nabi Biopharmaceuticals, calcium acetate), and Renagel all will have a role." The other doctor said, "We're just starting to hear about it. The sales reps are just starting to tell us about it."
- A Georgia nephrologist said samples had arrived at her office, and she gave samples to one hard-to-treat patient.
- An Arkansas doctor said, "I got an email survey the other day asking if I had heard of Fosrenol. I said no, and the response was, 'Thanks for participating in our survey.' I have no idea about how I'll use Fosrenol without detailing."
- Not a single doctor interviewed has written a prescription for Fosrenol yet – and none plan to do so until and unless they are detailed.

Doctors are interested in Fosrenol, and most said they probably will try it – but not until they are detailed. Thus, there is no pent-up demand or waiting list for Fosrenol. Furthermore, sources said they have no idea how they will use Fosrenol with respect to Renagel or how Fosrenol usage will be impacted by Medicare reimbursement changes in 2006. Initially, they plan to try Fosrenol on a few patients and see how those patients do. Doctors were unaware of any countermarking going on by Genzyme – yet – and the Genzyme sales reps at the meeting were not discussing Fosrenol with doctors.

GENZYME'S Renagel (sevelamer hydrochloride)

Doctors estimated that 50%-80% of their ESRD patients are on Renagel, and that percentage is expected to stay relatively constant over the next year in the U.S. but increase in Europe.

The main impediments to greater Renagel use are:

- **Pill burden.** A speaker said, "Even when patients are getting the drug for free, they are still petering off, so compliance is a major issue."
- **Cost.** This is as much or more of an issue as the pill burden, doctors explained. One said, "A lot of patients have insurance coverage for Renagel. People don't pay out-of-pocket for it, but most are on dialysis, and it is paid for." A nurse practitioner added, "Cost is the No. 1 problem, but even when you can get the pills, patients object to the number of pills."

The DCOR trial is comparing Renagel to calcium, with morbidity and mortality endpoints. There are four possible outcomes to this trial:

- Only a mortality benefit.
- Only a morbidity benefit.
- Benefits in both mortality and morbidity.
- No benefit in either mortality or morbidity.

Doctors said the trial would be a home run if it shows a statistically significant benefit on both mortality and morbidity, but even if it showed only a mortality or only a morbidity benefit, that would spur usage. Among the comments on the DCOR trial were:

- *Arkansas:* "The trial will absolutely have to show a mortality benefit, not just morbidity."
- "If there is only a morbidity benefit, my use might go up for some patients – those with co-morbid conditions where it would improve quality of life. But if there is a mortality benefit without a morbidity benefit, my use won't go up."
- *New York:* Both mortality and morbidity need to go down for that trial to be a success. Mortality alone is not enough; they also need to show a morbidity benefit."
- *Wisconsin:* "Use will go up if there is either a morbidity or a mortality benefit, but it will be best if there are both."
- *California:* "Mortality alone would be great. Morbidity alone would still be good, especially if the trial bears out the anti-lipid effect. Both would be great. Genzyme can't lose with the study unless it shows patients are worse with Renagel."

Genzyme was emphasizing its REACH program, which provides Renagel to low-income Medicare patients for only $25 a month through several of the Medicare drug discount cards. A source estimated that 30%-40% of ESRD patients have no prescription coverage, and about 7%-10% qualify for Medicare discount cards. Several nephrologists praised Genzyme for this program.

NABI BIOPHARMACEUTICALS' PhosLo (calcium acetate)

Many nephrologists continue to use PhosLo because it works, they have experience with it, and it is less expensive than Renagel.

- *Midwest:* "There is no hard evidence to say you should switch all your patients to Renagel, and PhosLo is cheap. PhosLo works very, very well. The only limitation is high calcium level."
- *Arkansas:* "It works, and it works well. It's been around a while, and I have a comfort level with it. Cost is not a big issue; it comes up, but it is not a major reason I prescribe PhosLo."
- "I use PhosLo because I'm familiar with it. I was trained with it, and I've seen it work."
- *Wisconsin:* "I start with PhosLo because of cost, when a patient can't take PhosLo or the Ca x P is increased, I switch to Renagel."

NEPHRO-TEC'S MagneBind

This magnesium binder was not required to go through the FDA approval process, but a prospective study is underway, with data expected in about a year and a half. However, doctors appeared dubious about the product.

INDUSTRY ISSUES:
DAVITA'S Purchase of GAMBRO HEALTHCARE

If Davita's purchase of Gambro goes through, which experts believe is likely, the combined company will be treating ~96,000 dialysis patients. Davita has a pretty good reputation, sources (doctors, nurses, and competitors) all agreed. They described Gambro as "poorly run" but have been impressed with the leadership at Davita.

On the positive side:

- *Competitor #1:* "The Davita/Gambro merger is very good for both companies. Gambro was in trouble, and the Davita leadership is very strong and will be able to raise money on Wall Street. But the merger is neutral to the industry."
- *Michigan:* "Hopefully, this will make things more efficient…Davita is bottom-line oriented."
- *Competitor #2:* "Depending on the part of the country being examined, from 88%-92% of dialysis patients are covered by Medicare. The profit is in the private-pay patients, not the Medicare patients. The advantage of a large company is you can spread the Medicare patients out. Large size also helps in negotiations with managed care companies…The merger also can give them more resources, expertise, and access to technology."

- *California:* "It's probably a good move because of the possibility of economics of scale…Davita has had good programs and high standards – higher than Gambro… We've had a partnership in Southern California with a couple of Davita clinics for 7-8 years, and that has worked very well. Davita knows what it is doing and is focused."

On the negative side:

- *California:* "We like more than one provider for bargaining power, and Davita really stretched itself with this."
- *Florida:* "Davita/Gambro may be too big to be manageable."
- *Competitor:* "The question will be whether Davita can merge the two cultures, which are very different. That is the hurdle. Gambro has old policies, and nephrologists and staff who have been there a long time. Davita is newer, and has a very aggressive leader. But you can't switch staff easily. There is also a lot of overlap between the two companies, and Davita will have to make decisions about what to merge, what to divest – and there are a lot of politics involved with the practicing nephrologists."

NEPHROPATHY

KERYX BIOPHARMACEUTICALS' sulodexide (KRX-101)

Doctors agreed that ACE inhibitors and ARBs are considered good and effective therapies for early as well as late stage diabetic nephropathy. ACEs and ARBs are started as soon as patients show signs/symptoms of diabetic nephropathy.

There was little excitement about oral sulodexide, a first-in-class oral heparinoid (a glycosaminoglycan). Sulodexide has been marketed in Europe, South America, and Asia for more than 20 years, but it is not yet approved in the U.S. Sources all agreed that the drug will need to show superiority to placebo on top of background therapy with either an ACE or an ARB.

Sources were not familiar with the DiNAS trial, which was published in 2002. In this 223-patient, European, Phase II study, patients with diabetic nephropathy were treated daily for four months with sulodexide (at 50 mg, 100 mg, and 200 mg) gelcaps. Researchers reported that 42% of sulodexide patients achieved normalized albuminuria vs. 14% on placebo.

In early January 2005, Keryx announced that it was proceeding to a Phase III trial, based on an interim analysis of an ongoing 150-patient, randomized, double-blind, placebo-controlled Phase II trial. The company expects to start a pivotal, Phase III in microalbuminuria as well as a Phase IV trial in macroalbuminuria by about April 1, 2005. Keryx has been granted accelerated approval by the FDA. Both trials are on top of maximum ACE/ARB therapy. The pivotal trial includes six months of drug therapy followed by two months off-therapy.

Radiocontrast-induced nephropathy

The increased use of CT scans, and thus, contrast agents, raised the question of whether there has been an uptick in radiocontrast-induced nephropathy. However, nephrologists said this does not appear to be a growing problem for several reasons:

- **Dialyzing after use of radiocontrast.** A Texas nurse said, "We always dialyze after radiocontrast. The radiologists want it, but I'm not sure it does any good. The dialysis will sometimes kick people on the edge of ESRD over the edge."
- **Hydration.** A source said, "The role of hydration is key. There is no real concern about increased nephropathy with CT, but there is increased awareness of the importance of prevention." A Louisiana doctor said, "Most doctors are aware of what to do to prevent nephropathy – hydration, using less contrast material, using more physiologic concentrations of contrast, and being extra careful with diabetics, the elderly, and patients with renal problems. Radiologists also are consulting nephrologists."
- **Minimizing the contrast dose.**

THE REGULATORY PERSPECTIVE

Dr. Barry Straube, Chief Medical Officer for CMS's Region 9, a consultant to CMS nationally on ESRD, and the only nephrologist or transplant physician at CMS, discussed regulatory issues. Among the points he made were:

- There is wide variation among the dialysis chains over the percent of patients achieving Hgb>12. Davita, for example, has 60% of patients achieving Hgb>12, but Fresenius and Gambro have very, very few with Hgb>12. He said, "For-profit facilities have a greater number of patients getting Hgb>12 vs. non-profit, hospital-based, and freestanding centers."
- The Government Accounting Office (GAO) and the Office of the Inspector General (OIG) are holding CMS more accountable.

Dr. Straube cited what he called "several unaddressed quality issues":

- **Why is there so much geographic variation in measures?** There has been tremendous growth in for-profit dialysis units, with wide geographic variation across the country.

- **Why are health disparities largely ignored,** especially racial and ethnic disparities? The growth in dialysis is disproportional with respect to African-Americans.
- **How do reimbursement policies affect the quality of care?**
- **Why are covered services – such as vaccinations – not provided?** The goal is to have 75%-100% of ESRD patients vaccinated for flu and pneumonia, but, again, there are wide variations by chain. Gambro was lowest on vaccinations shots, and Renal Care Group highest. Dr. Straube said, "These are a separate Medicare benefit, so there is no excuse for not giving them." Hepatitis B vaccination rates for staff also show quite a bit of variation, with Davita ~85% and Gambro lowest at ~82%.
- **Why is PD not more widely utilized?**
- **How transparent should the ESRD program be?** What should be reported to the public?

CMS's annual report on clinical performance measures is typically issued in late March or early April, but a number of new measures to be utilized already are being worked on. Dr. Straube recommended watching the CMS website for news on:

- Bone disease measures.
- Referral of patients for transplantation.

Priorities for CMS chief Dr. Mark McClellan were described as:

- **Economics as well as quality.**
- **Conditions of coverage of ESRD facilities.** This guidance has been expected for a long time; there have been no changes since the mid-1970s, but Dr. Straube said there is a "very, very high probability" of coming out at the end of January 2005. Among the items likely to be in the document are:
  - **Tougher oversight of large dialysis organizations** since the GAO and OIG issued a number of reports over the last year saying CMS was not holding large dialysis companies accountable for existing regulations.
  - **More focus on outcomes.**
  - **Facility medical director accountability.** Dr. Straube said, "Unequivocally, OIG, GAO, and Congress sent a message in their independent investigations that medical directors need to play a greater role in monitoring care and doing other functions in dialysis facilities."
- **Quality issues, including**:
  - Continuation of monthly capitative payments.
  - Announcing a bundled payment system.
  - ESRD demonstration project. CMS hopes to get this underway some time in 2005.
  - Pay for performance. Dr. Straube predicted, "You will hear more about that."
  - Healthcare information technology. He said, "You will hear more about that, too."

THE WALL STREET PERSPECTIVE

A Morgan Stanley analyst was the speaker at a session on "The View from Wall Street." His renal-related predictions included:

- 2005 will be a slowdown year, but he said that defensive sectors such as pharmaceuticals tend to do better in that environment.
- 2005 investments should focus on companies with stable growth, pricing power, and which are reducing debt or returning cash to shareholders. He said dialysis stocks meet all three criteria: They have growth, good pricing power with insurers (neutral with the government), and are generating good cash flow.
- At the end of 2005, market share will be: 31% Davita/Gambro, 26% Fresenius, 10% Renal Care Group, and 33% other.
- International services are an emerging market opportunity.
- In the dialysis products area, no major shifts or disruptive technologies appear close to market.
- Consolidation will continue in the U.S. dialysis services sector, and consolidation of smaller clinics may accelerate in 2005 and 2006. Consolidation may provide more pricing power for clinics.
- The three for-profit dialysis center business models in the U.S. are:
  - **Fully vertically integrated.**
  - **Quasi-vertically integrated** – e.g., Davita. He called this the least attractive model because lower costs are not necessarily passed on to the services business, "But Davita probably thought they needed critical mass in this market."
  - **Stand-alone service business** – e.g., Renal Care Group. This doesn't require significant capital invest-ment in a manufacturing plant, and it is probably better for a business located in a single geography.
- Larger chains are likely to differentiate their product offering. He said, "There is a clear difference between Fresenius and Davita with respect to single use and re-use. Fresenius went just single-use, and Davita will be on a re-use schedule if it uses the Gambro approach. What

impact that will have on physician referrals is hard to understand."

- Longer-term chains will want to find new revenue streams for offering additional services, which may ultimately be a positive for patients.
- Labor costs are now a major mid-term concern. Centers need more medical directors and dialysis nurses, and in five years centers could be fighting for the best staff – or paying more for doctors and nurses.
- Large for-profit chains will continue to make a margin on drugs because large companies should be able to purchase drugs below average price due to volume.

- The margin squeeze on EPO has been removed. EPO reimbursement will be updated annually instead of requiring a legislative change.
- High drug-use clinics may lose out initially as the drug profit is taken away.

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